THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES.

SEPTEMBER, 1903.

ACUTE MYELOGENIC LEUKÆMIA.

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Acute leukæmia has become a well-known and generally recognized disease. Nearly always it is of the lymphatic type. The following case is of the myelogenic variety, and, therefore, is of more than ordinary interest:

The patient was a man, aged sixty-eight years, free from hereditary taint. He was abstemious in his habits, and gave no history of venereal infection. When fifty years old he suffered from nervous prostration. Nine years ago he was jaundiced from the passage of gallstones. Seven years ago he was subject to uræmic headache, brought on by Bright's disease. Four years ago a fistula in ano developed.

The present illness began in August, 1899, with an ulceration which formed at the root of a decayed tooth. Weakness and loss of flesh were present. The jaw-bone was carious. A blood examination was made at this time by Dr. R. C. Cabot, and showed a normal condition.

September 20th. The weakness had increased and the patient complained of anorexia, indigestion, constipation, and sleeplessness. The body was emaciated. Temperature slightly elevated. Marked pallor. The spleen could not be felt, and no hemorrhages were in evidence. The glands were not swollen.

Blood Examination. Hæmoglobin, 40 per cent.; leucocytes, 2,000,000; whites, 540,000. The stained specimens showed only moderate poikilocytosis and 2160 nucleated red cells to 1 c.mm., most of which were normoblasts. Small mononuclear leucocytes, 4 per cent.; large mononuclears, 39.2 per cent.; polynuclear neutrophiles, 24 per cent.; eosinophiles, 1.6 per cent.; mast-cells, 0.8 per cent. There were 30.4

per cent. of myelocytes, of which 2.4 per cent. contained eosinophilic granules.

The condition of the patient grew rapidly worse. Hemorrhages took place under the skin and from the gum in the region of the necrosed bone. The temperature daily reached 102° to 103°, and he sweat profusely. Œdema of the lungs appeared. Along with the progressive loss of flesh a mental hebetude developed.

By October 7th the anæmia had become very marked, and the gums were spongy and bleeding. Pulse rapid. The heart was moderately enlarged to the left, and a soft systolic murmur was heard at the apex; aortic second sound accentuated. The spleen was distinctly palpable one finger's breadth below the costal edge. Urine scanty, large amount of albumin, many granular and hyaline casts.

Death occurred from asthenia about two months after the onset. The last blood examination, on October 7th, showed hæmoglobin, 30 per cent.; erythrocytes, 1,700,000; whites, 374,000. In the differential count were 2618 nucleated red cells to 1 c.mm., most of them normoblasts. Small mononuclear leucocytes, 1.6 per cent.; large mononuclears, 22 per cent.; polynuclear neutrophiles, 21.2 per cent.; eosinophiles, 0.4 per cent.; mast-cells, 0.4 per cent.; myelocytes, 54.4 per cent., of which 0.8 per cent. were eosinophilic. Many free nuclei were scattered about in both specimens. The classification of myelocytes and large mononuclears was often arbitrary, since the granulations were frequently faint. The mononuclear cells corresponded in size and appearance to the myelocytes, save for the absence of granules. The large mononuclears varied in diameter from 14 to 20μ, while the myelocytes ranged from 12 to 20μ.

The close relationship between these two groups of granular and non-granular mononuclear cells is seen in both counts. The latter count has more myelocytes and fewer large mononuclears than the former, but the totals are only slightly altered (69.6 per cent. and 76.4 per cent., respectively). The later blood count might be looked upon as an older blood product than the earlier, as shown by the greater number of granular elements; but we think the difference is dependent chiefly on the technique of staining. By using a high heat the granules are not stained well; by using a lower temperature the granules are plain.

For many years leukæmia was looked upon as a disease that always ran a chronic course. Ebstein first called attention to the acute forms of leukæmia. Fränkel made an exhaustive study of all the cases in the literature in 1895, including ten cases of his own. He drew this important conclusion: That all cases of acute leukæmia are lymphæmias, in which the increase of white cells chiefly or almost exclusively consists of large or small lymphocytes. He does not admit the existence of an acute myelogenic leukæmia.

Pinkus states that all cases of acute leukæmia up to that time (1901) described were of the lymphatic type. Ehrlich and Lazarus in the same year also observe that no instance of undoubted myelogenous leukæmia running an acute course had yet come to their notice.

Pinkus and Lazarus incorrectly state that Cabot has reported two

probable cases. Dr. Cabot informs us, however, that all of his acute cases have been lymphatic.

Most writers on the subject have accepted the view of Fränkel.

Fussell, Jopson, and Taylor, in their review of fifty-six cases of acute leukæmia, consider the disease lymphatic, because in three cases only were myelocytes present to any extent.

Walz, however, enters a protest against classifying acute leukæmia as necessarily lymphatic, for the reason that "it is not yet certain that there are not cases of acute myelogenic leukæmia."

Grawitz, likewise, vigorously maintains that an acute leukæmia may rarely present either a mixed or a medullary blood finding.

Ewing clearly recognizes an acute myelæmia and points out its essential characteristics.

More recently Hirschfeld and Alexander have reported a case of unquestioned acute myelogenic leukæmia.

We have attempted to review the literature and critically select from it those cases which resemble the picture of acute myelogenic leukæmia. Many reports give such inadequate blood findings that they are not considered.

For the sake of convenience we have placed all the possible cases under two groups: 1. Clear cases of acute myelogenic leukæmia. 2. Probable cases of acute myelogenic leukæmia.

1. We have made a brief résumé of the clear cases:

Case I.—Van der Wey's case was a girl, aged twenty-three years, who had enjoyed excellent health in the past. Illness began with headache, dizziness, ringing in the ears, and pain in the left shoulder.

Status Præsens. Few swollen glands in the cervical, axillary, submaxillary, inguinal, and cubital regions, varying in size from a pea to a bean. Spleen palpable. Hæmoglobin, 60 per cent.; reds, 2,840,000; whites, 175,000. Most of the whites (60 per cent.) were myelocytes containing faint or distinct granules; 1.9 per cent. eosinophiles; few small mononuclears; polynuclears, 33 per cent.

Six weeks later the condition, hitherto stationary, became suddenly worse. Fever, repeated nose-bleed, loss of weight, and rapid anæmia occurred. Hæmoglobin, 22 per cent.; reds, 900,000; whites, 300,000. The large mononuclears predominated, although myelocytes were still abundant. Polynuclears fell to 3.7 per cent.; eosinophiles to 0.3 per cent. The large mononuclears and myelocytes together constituted 96 per cent. of all the white cells. The small mononuclears were few. Death three months after illness began.

Autopsy. Slight enlargement of external and internal glands. Marrow soft, gray, and looked like a mixture of pus with blood.

Van der Wey inclines to call this case a transformation of a chronic myelogenic to an acute lymphatic leukæmia, since the granular elements (myelocytes) were largely replaced by the non-granular (large mononuclear). Without question the large mononuclear cells were

myeloid cells, some containing faint granules, which explains his difficulty in separating them from the myelocytes.

Thompson and Ewing report the following case :

CASE II.—A woman, aged twenty-one years, with no history of syphilis or other severe illness. For six months had experienced frontal headache, but was in fair health until six weeks previous, when she was taken with sore throat that lasted two weeks. Then the right arm became swollen, red, and painful, and remained so for three weeks. Three days before observation she fainted and fell, striking the left side, after which she suffered from severe pain in the abdomen. Later she had repeated attacks of vomiting, and of fever, ranging from 102° to 105°. The only hemorrhage evident was in the skin of the nose. The spleen was scarcely palpable. No enlargement of the lymph glands. Death took place eleven days after the first examination, and less than eight weeks from the probable initial symptom.

The blood count, made two days after admission, was 1,290,000 red cells; hæmoglobin, 20 per cent. Marked leucocytosis, estimated at about 50,000. Of the leucocytes 5 per cent. were myelocytes of medium size. No nucleated red cells seen. Five days later, whites about 100,000; mononuclears, 33 per cent.; polynuclears, 55 per cent.; myelocytes, 12 per cent.; occasional eosinophiles and abundant normoblasts. After death, mononuclears, 17 per cent.; polynuclears, 48 per cent.; eosinophiles, 0.3 per cent.; myelocytes, 17 per cent. No mast-cells. The granules of the myelocytes were often indistinct.

Post-mortem. Leukæmic deposits in the spleen, liver, abdominal lymph nodes, and marrow. Microscopically the marrow showed entire absence of fat-cells and a diffuse growth of myelocytes.

This case is a typical acute myelæmia, as was recognized by the authors at the autopsy.

CASE III.—Grawitz gives the history of a spinster, aged forty-two years, whose health was previously good. The onset was marked by long-continued hemorrhage following the extraction of fourteen teeth at one sitting. The patient entered the hospital with a severe stomatitis and necrosis of the jaw. On account of the great prostration, retinal hemorrhages, and enlargement of the spleen, the diagnosis was made of acute leukæmia. The cervical glands were moderately swollen. The spleen extended three fingers below the costal edge.

Leucocytes, 190,000; small mononuclears, 5 per cent.; large mononuclears, 15 per cent.; polynuclears, 10 per cent.; 60 per cent. were neutrophile and 10 per cent. eosinophile myelocytes, or 70 per cent. of myelocytes in all.

Death took place in two weeks.

Grawitz calls the case "an outspoken medullary or mixed blood picture in a very acutely progressing leukæmia."

CASE IV.—Ewing describes the case of a middle-aged negro who, for two months, was ill with gingivitis, hemorrhages from the mouth and bowels, fever, and progressive anæmia. The superficial glands were not much enlarged. The spleen was moderately increased in size. This case was correctly diagnosed as acute leukæmia during life by

means of the marked leucocytosis and the great number of neutrophile myelocytes. The patient died with symptoms of sudden collapse and enormous tympanites. Soon after death there was rapid gaseous decomposition due to the bacillus aërogenes capsulatus. The bone-marrow was puriform.

CASE V.—A second case of Ewing was a young man whose illness ran a rapid course. The glands and spleen were slightly enlarged. Hæmoglobin, 20 per cent.; reds, 1,080,000.

Post-mortem. The blood collected from the axillary vein showed 686,000 erythrocytes, 31,000 leucocytes. Mononuclears, mostly small, 61 per cent.; neutrophilic myelocytes, 31 per cent.; eosinophilic myelocytes, 2 per cent.; polynuclears, 6 per cent., and a few mast-cells. Nucleated reds moderately abundant; usually of small size. No distinct megaloblasts. Moderate difference in size of red cells. Smears from the marrow show chiefly myelocytes.

In the lymph glands was a uniform growth of large mononuclear cells, non-granular. The spleen showed many small lymphocytes.

Both of these cases Ewing considers are acute myelæmias, as determined by ante-mortem and post-mortem findings.

CASE VI.—Hirschfeld and Alexander narrate their observation of a man, aged twenty-one years, whose illness began with a swelling in the foot. Soon after a swelling of the under jaw came on, treated by extraction of the tooth. The wound bled profusely, and later an ulcer formed. Submaxillary glands slightly swollen, but the spleen was not palpable. At the first examination the hæmoglobin was 35 per cent., reds 2,000,000, no quantitative nor qualitative change in the white cells. Rapidly the pallor increased, and there was a moderate fever.

In the course of five weeks the spleen and glands steadily grew larger; the leucocytes increased, to 64,000; the hæmoglobin fell to 10 per cent. and the reds to 1,125,000. By differential staining it was seen that the large mononuclears varied from 16 to 20 per cent. and the myelocytes from 5 to 8.6 per cent. Normoblasts present in small number. Death occurred two months after the onset.

Post-mortem. The bone-marrow consisted chiefly of myelocytes and large mononuclears. The spleen tissue was made up almost entirely of granular cells, as well as giant cells. Smears of the spleen were in no way different from those of the bone-marrow. The glands also showed an infiltration of myelocytes. The ulcer of the jaw showed a compact cell mass consisting of myelocytes, polynuclears, and eosinophiles.

CASE VII.—Michaelis publishes an account of a woman in her fiftieth year. Pneumonia and peritonitis were the only important previous ailments. She passed the menopause at forty. The onset of her illness was ten weeks preceding entrance to the hospital. She complained of dulness, cough, expectoration, and a stitch in the left hypochondrium, which steadily increased.

Status Præsens. No glandular enlargement. Throat, mouth, and tonsils normal. There was slight fever. The spleen almost filled the left side of the belly and was soft. Urine negative.

Dulness, dyspnœa, and pain in the splenic region progressed gradually, and the skin grew paler. Excepting for slight hemorrhages in the retina, the objective findings remained unaltered. Hæmoglobin, 40 per cent.; reds, 3,450,000; whites, 16,000; slight poikilocytosis; small

mononuclears, 20 per cent.; large mononuclears, 56 per cent.; polynuclears, 16 per cent.; eosinophiles, 0.4 per cent.; mast-cells, 0.4 per cent.; neutrophile myelocytes, 7.2 per cent.; normoblasts in moderate numbers. Later both small and large nucleated reds were more numerous.

Death in fifteen weeks from beginning of symptoms.

Autopsy. The bone-marrow contained large numbers of giant granular cells and large mononuclear cells without granules. Myelocytes not so numerous. Marrow cells likewise were found in the lymph glands and spleen.

Michaelis gives cuts illustrating the large mononuclear cells in various stages of transition to the myelocytes.

2. The only cases that seem to fall into this group of probable acute myelogenic leukæmia are the following:

CASE I.—Obrastow reports the case of a seventeen-year-old schoolgirl, whose illness began with nose-bleed and fever. The spleen, at first scarcely palpable, grew rapidly larger until it was a hand's breadth below the ribs. Moderate swelling of cervical, axillary, and inguinal glands. The hæmoglobin fell to 30 per cent.; reds, 3,044,000. The leucocytes at the beginning were increased, and before death were in the ratio of 1 to 7 erythrocytes. Myelocytes were present. Death ensued in two weeks after the onset. On post-mortem a diphtheritic inflammation of the soft palate was found, a colitis, and pus cocci in the glands.

CASE II.—Patient was the nurse of the previous case. Six weeks after her death was taken with fever and inflammation of the hard palate. Then petechiæ, albuminuria, and enlargement of the spleen developed. Only the glands about the jaw were swollen. White cells 1 to 9 reds. Later the spleen reached the navel. Myelocytes with faint granules seen. Death in thirty days from the first symptoms.

Both of these cases appear to be infectious, and in both myelocytes were found, but their number is not stated.

Fränkel thought that the large mononuclear cells with faint granules were lymphatic cells, and includes both cases in his series of acute lymphatic leukæmias.

These cells seem to us, however, to be true myelocytes.

CONSIDERATION OF SYMPTOMS. Most of the eight clear cases (see table) began abruptly in the manner of an infection; four cases had a throat inflammation, and in three there was a necrosis of the jaw or palate. With two exceptions the glands were slightly or moderately enlarged, the cervical group being usually affected. The spleen was always large enough to feel. In only two instances, however, was the edge more than one finger's breadth below the costal margin. Hemorrhages occurred in every case where the history was obtained. Fever was present in most cases, of an irregular, low-grade type. The anæmia was always severe and rapid. Yet poikilocytosis was usually less marked than in a pernicious anæmia correspondingly severe. The

white cells varied from 16,000 to 540,000. The average count is much lower than ordinarily found in the chronic myelogenic leukæmia.

DIAGNOSIS. A number of conditions bear a resemblance to acute myelogenic leukæmia, and some of them have been wrongly described as such. Among the more important sources of error may be mentioned:

1. *Chronic Myelogenic Leukæmia with Acute Exacerbation* (Reimann). The blood picture is quite similar to the acute myelogenic leukæmia, but the patient gives a history of a long-standing illness, and at the first examination a large splenic tumor is present, whereas in the acute type the spleen is scarcely palpable in the first stages.

2. *A Lymphatic Leukæmia Complicated by Some Intercurrent Infection* (Hirschlaff). The appearance of many neutrophile polynuclear cells makes an unusual picture. Myelocytes, however, are few or wanting altogether.

3. *Acute Lymphatic Leukæmia where the Large Mononucular Cells Predominate.* Selig has described such a case as an "acute mixed leukæmia" on the ground that these cells are from the marrow. In the entire absence of myelocytes this diagnosis is untenable.

4. *Acute infections* associated with a grave and rapid anæmia may give rise to nucleated red corpuscles and myelocytes. Leube reports a case where 14 per cent. of a white count of 10,500 consisted of myelocytes. Yet he regards it not as leukæmia, but as an infection with irritation of the bone-marrow. The white count generally is much lower than in acute myelogenic leukæmia.

5. *Acute exacerbations of pernicious anæmia* may be mistaken for a myelogenic leukæmia, if the blood has not been previously examined. As an illustration of such a blood picture we cite a pernicious anæmia case reported by Billings where two days before death the white count was 34,000, and included 29.4 per cent. of myelocytes.

6. *New-growths involving the bone-marrow* cause blood changes somewhat similar to leukæmia. Myelocytes and nucleated red cells are both present. Türck within the last year was able to correctly diagnose a case in Neusser's clinic during life. He based the conclusion on the enormous number of nucleated red cells present in the blood of both cases. In one case there were over 90,000 per c.mm. Myelocytes were not very numerous. Confusion of marrow neoplasm with acute myelogenic leukæmia is unlikely, because the former runs a chronic course and the anæmia is gradual.

The *differential diagnosis* between acute myelogenic and acute lymphatic leukæmia cannot be made either by the clinical symptoms, the physical findings, or even by the ordinary count of white cells. In all these respects the disease may be identical with acute lymphatic leukæmia. Only by means of differentiating the white corpuscles in a

stained specimen can the type be identified. If the lymphocytes prevail we call the disease lymphatic; if the marrow cells predominate, we call it myelogenic. And herein lies a great difficulty: to determine whether certain cells are of lymphatic or myelogenic origin.

The school of Ehrlich draws a sharp line between the non-granular lymphatic cells and the granular myeloid cells.

Pappenheim, Walz, and their followers believe that the marrow produces all of the myelocytes and large mononuclear "mother cells," all of the neutrophile and eosinophile polynuclear leucocytes, and a certain proportion even of the small lymphocytes. They consider all leukæmias myelogenic with or without a participation of the glands. In favor of this view it is asserted that every well-studied case of lymphatic leukæmia has shown post-mortem an involvement of the bone-marrow. At the same time they concede that both small and large mononuclear cells may also come from the lymph glands.

Naegeli thinks the lymphatic large mononuclear cell can be morphologically distinguished from the myeloid cell or "myeloblast" by its appearance alone.

In practice it is often impossible to say whether the large mononuclear cell is to be classed among the large lymphocytes or the unripe myelocytes. The myeloid cell has usually an eccentrically placed nucleus; the nucleus is often oval; the protoplasm is often faintly granular. We would suggest this as a safe rule to follow: When large mononuclear cells are seen with a considerable number of myelocytes of the same size, and when many of the mononuclears show indistinct granulations, they may be considered as myeloid cells.

In all of the recorded cases of acute myelogenic leukæmia there was difficulty in separating the large mononuclears and the myelocytes, because so many transitional cells with faint, indistinct granules were present. The large mononuclears never were less than 15 per cent., while the myelocytes varied from 8.6 per cent. to 60 per cent. The small mononuclear cells were relatively diminished. Eosinophiles were either absent, present in small number, or increased. Mast-cells were seen in one case only. Nucleated red corpuscles did not form an essential part of the picture, as in the chronic myelogenic type.

Using the published cases as a basis, the blood picture of acute myelogenic leukæmia may be summed up as follows:

1. Anæmia, progressive and severe.
2. A large increase of white blood corpuscles (16,000 to 540,000).
3. A large proportion of the white cells (25 to 96 per cent.) made up of myelocytes, large mononuclear cells of the same size, and faintly granular large mononuclear cells (transitional cells).
4. Eosinophiles, mast-cells, and nucleated red corpuscles may be absent or present in varying numbers.

No.	Observer.	Sex. Age.	Duration.	Mouth Infection.	Glands.	Spleen.	White Count.	Differential Count of Leucocytes.
1	Van der Wey, 1896	F. 23	3 months.	None.	Cervical, submaxillary, and inguinal vary in size from pea to a bean.	Palpable.	175,000 to 300,000.	Few small mononuclears; polynuclears, 33 per cent.; eosinophiles, 1.9 per cent. Myelocytes, 60 per cent., containing faint and distinct granules.
2	Thompson and Ewing, 1898	F. 21	8 weeks.	Sore throat.	Normal.	Scarcely palpable.	50,000 to 100,000	Polynuclears, 3.7 per cent.; eosinophiles, 0.3 per cent.; mononuclears and myelocytes, 96 per cent. The large mononuclears predominate, although myelocytes are plentiful.
3	Grawitz, 1900	F. 42	2 weeks.	Stomatitis; necrosis of jaw.	Moderate enlargement of cervical group.	3 fingers below costal border.	190,000.	At first, myelocytes, 5 per cent.; five days later, lymphocytes, 33 per cent.; polynuclears, 55 per cent.; myelocytes, 12 per cent.
4	Ewing, 1901	M. 34	months.	Gingival hemorrhage from mouth.	Slightly enlarged.	Moderately enlarged.	Marked increase.	After death: Lymphocytes, 17 per cent.; polynuclears, 48 per cent.; eosinophiles, 0.3 per cent.; myelocytes, 17 per cent.; many with indistinct granules.
5	Ewing, 1901	...	Acute course.	Not stated.	Slightly enlarged.	Moderately enlarged.	31,000.	Small mononuclears, 61 per cent.; polynuclears, 6 per cent.; neutrophile myelocytes, 31 per cent.; eosinophile myelocytes, 2 per cent. Few mast-cells.
6	Hirschfeld and Alexander, 1902	M. 21	2 months.	Necrosis of hard palate.	Cervical, size of pea to pigeon's egg.	One finger below costal border.	42,000.	Small mononuclears, 7.4 per cent.; large mononuclears, 19.2 per cent.; polynuclears, 63 per cent.; eosinophiles, 0; myelocytes, 8.6 per cent.
7	Michaelis, 1902	F. 50	15 weeks.	None.	Normal.	Very large.	16,000.	Small mononuclears, 20 per cent.; large mononuclears, 56 per cent.; polynuclears, 16 per cent.; eosinophiles, 0.4 per cent.; mast-cells, 0.4 per cent.; neutrophile myelocytes, 7.2 per cent.
8	Billings and Capps.	M. 68	2 months.	Caries of jaw.	Slight enlargement of the cervical.	One finger below the costal border.	540,000 to 874,000.	Small mononuclears, 4 per cent.; large mononuclears, 39.2 per cent.; polynuclears, 24 per cent.; eosinophiles, 1.6 per cent.; myelocytes, 30 per cent.; mast-cells, 0.8 per cent.
								Small mononuclears, 1.6 per cent.; large mononuclears, 22 per cent.; polynuclears, 21.2 per cent.; eosinophiles, 0.4 per cent.; myelocytes, 54.4 per cent.; mast-cells, 0.4 per cent.

ADDENDUM. Since this article went to press another case has been reported by Türck (*Zeitschrift f. innere Medicin*, No. 13, p. 336), under the title "Acute Myeloid Leukæmia." The duration was not stated. The blood findings were: hæmoglobin, 19 per cent.; erythrocytes, 1,060,000; whites, 42,000. The leucocytes consisted of 14 per cent. lymphocytes, 32 per cent. polynuclears, 47 per cent. myelocytes. Post-mortem the bone-marrow was of grass-green color, and was made up almost exclusively of neutrophile myelocytes and transitional forms.

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TUMOR OF THE INTERCAROTID BODY.

A REPORT OF ONE CASE, TOGETHER WITH ALL CASES IN LITERATURE.

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FIVE cases of tumor of the intercarotid body are recorded in medical literature. Paltauf[1] reports four of these with a most exhaustively systematic study of the structure, development, and pathology of the intercarotid body. Marchand records one case of tumor of this same intercarotid body. These five cases, with the one recorded in this paper, constitute all the known instances in medical experience. The case which I have to report is as follows:

The patient was a woman between twenty and thirty years old. The diagnosis had been made of an enlarged gland in the neck. There was no history of tuberculosis in the family. The woman was well

[1] Beiträge path. Anat. Allgem. Pathologie. Ziegler, Jena, 1892.

developed and well nourished. For over nine years she had noticed a small bunch in the right side of the neck. This bunch had increased slightly in size and had become tender whenever she had a cold.

Examination found upon the right side of the neck, in front of the middle third of the sternomastoid muscle, and lying partly in the submaxillary and superior carotid triangles, a firm, non-fluctuating, non-tender tumor, the size of a pigeon's egg. The tumor was slightly

FIG. 1.

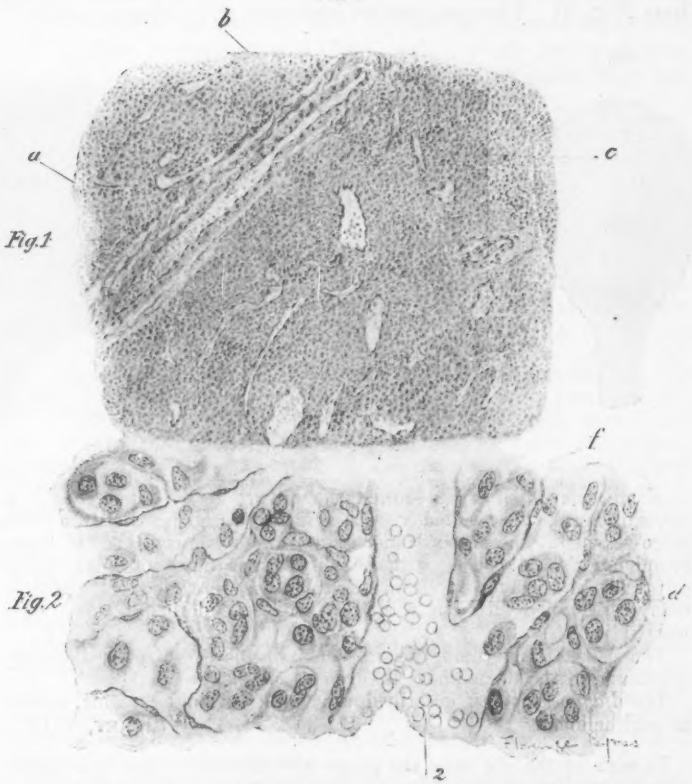


FIG. 1. *a*, tumor cells; *b*, endothelial cells seen lining the blood space; *c*, tumor cells.
FIG. 2. *d* and *f*, tumor or parietal cells: 2, red cells of the blood within the vascular space.

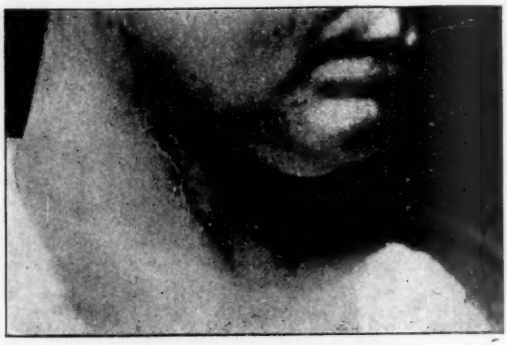
movable from side to side. The skin was movable over the tumor. Pulsation was felt, but no expansile impulse noted.

Operation. Incision over the tumor. It was uncovered, and found to be highly vascular. Blood oozed from it when touched with the forceps. The common carotid artery was continuous with the sheath of the tumor. The tumor could not be separated from the artery. The common carotid was ligated above the anterior belly of the omo-

hyoid in two places, and divided between the ligatures. After the ligation of the common carotid the oozing continued, and a ligature was placed about both the internal and external carotids, for it was now evident that the tumor was intimately connected with these two vessels. Upon placing this ligature the oozing ceased, and the tumor was removed with the vessels. (See Fig. 3.) The patient recovered without incident from the operation. She complained of some sore throat the following day. The temperature rose to 99.2° F.; the pulse gradually declined from 110 to 80; the respiration dropped from 25 to 20. There has been no recurrence after thirteen months.

FIG. 2.

FIG. 3.



Cicatrix after removal of intercarotid tumor.

Microscopic examination showed the growth to be traversed by a series of large, thick-walled vessels, evidently arteries. Between these large vessels lay the proper tumor tissue, which was composed of large, round, and spindle cells, with but little appearance of intercellular substance, and traversing it in all directions were blood channels, in many cases lined with but a single layer of endothelial cells. (See Figs. 1 and 2.)

The cells of the tumor mass seemed in places to have distinctly originated in the tissue about these small vessels.

The *diagnosis* is best described as a variety of angiosarcoma, known as perithelioma.

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In each of the six cases the tumor was situated in the fork of the common carotid artery. It had so developed that neither the internal nor the external carotid could be separated from it. The tumor could be separated from the surrounding tissue, but not from the vessels.

The tumor was more or less circumscribed by a connective tissue capsule. It was nourished by vessels arising from the carotids directly. The tumor appeared in the superior carotid triangle and lower part of the submaxillary triangle. It rarely became larger than a hen's egg. I was mistaken for an ordinary lymphoma or an aneurism.

These tumors are not without danger. They may grow to large size, and become destructive in character to surrounding tissues.

In one case the vessel wall had been so invaded as to cause secondary hemorrhage.

In one case, on the fifth day following the operation, there appeared hemiplegia, right facial and hypoglossal paralysis, together with aphasia. The patient recovered from all the paralyses. The aphasia was the last to disappear.

Two years after the operation there had been no return of the growth.

In another of these cases a slight paresis of the left vocal cord remained for some time. Four years after the operation there was no return of the tumor, and the patient was well.

In one of the cases recorded there was a return of the tumor one year following operation. The recurrent tumor was removed, but was not recorded or examined.

Marchand's case is reported as follows. It resembles closely the case recorded above:

Marchand's[1] case of a tumor of the intercarotid body occurred in a woman, aged thirty-two years, who had observed the mass for four and one-half years; it was on the right side. Up to the age of twenty-two years the patient had been an epileptic. After that she had suffered from severe headaches, though not especially on the right. She desired the operation, though she had never been troubled by the tumor. Her pupils were equal, the color on both sides of the face was equal, and there were no symptoms referable to the sympathetic. About the tumor, which was the size of a hen's egg, and under the angle of the jaw pulsation existed in all directions. A lymphoma was at first diagnosed.

At the operation the carotid was found to be so surrounded by and embedded in the tumor, which was fitted into the bifurcation, that to remove the mass it was necessary to tie off the vessels. The patient died on the third day of bronchopneumonia. The vagus was cut at the time of operation. Autopsy showed no metastases.

Microscopically. In many places the tumor tissue, consisting of great polyhedral cells, was directly in contact with the endothelium of the blood spaces with no tissue substance intervening. It seemed as if the whole tissue by a gradual disappearance of fibrillar substance and increase in cell elements was being transformed directly into foci of thickly crowded together cells.

The tumor cells accordingly must be held to originate from the subendothelium or perithelium. The great resemblance to epithelium of the groups of cells in the alveoli is due to their close crowding and their consequent flattening. It can hardly be doubted that the cell growth which led to the tumor formation must have originated from the cell elements forming the principal part of the single lobules or kernels of the little organ, and which enclose the numerous vessels like a thick mantle.

[1] Festschrift f. Rudolph Virchow, Bd. 1. S. 547.

The growth was doubtless malignant from the degenerative effect it exerted on the neighboring nerve trunks, and from the formation of small, gray nodes of cellular outgrowth which projected into the lumen of the carotid, in spite of the fact that the tumor was in general sharply marked off from its surroundings.

"I have not given a name to the tumor, because I know of none which exactly fits. One would seem most justified, in view of its structure and etiology, in calling it an alveolar angiosarcoma."

The main interest of the peculiar growth doubtless lies in its origin from the characteristic elements of a structure which in man at least seems to possess the significance of a rudimentary organ.

The tumor was the size of a hen's egg, 5.5 x 3.8 x 3.5 cm. It completely enclosed the carotid, which bifurcated in its midst. On section it was seen that the internal carotid soon after being given off was much narrowed and thrombosed. Through the growth passed the sympathetic, which showed degenerative pressure changes. The vagus passed down to one side, and the hypoglossus through the tumor.

The peculiar relation of the tumor mass to the trunk and main branches of the carotid made one suspect that this unusual growth could have originated from no other structure than the so-called glandula carotid. The near relation to the sympathetic spoke also in favor of this etiology. Examination of the cross-section made this seem even more probable, since no glandula carotid could be found in its normal position, and, furthermore, the porous, apparently oldest portion of the growth next to the internal carotid occupied the exact position of that little structure.

For this reason the other side of the neck was examined and the glandula carotid was found in its normal position in the carotid notch, the size of a kernel of corn.

A word as to the histological findings of the intercarotid body will be of interest, as so little is generally known of its structure.

Paltauf finds that the intercarotid body is surrounded by a thick, partly fibrillated, partly homogeneous, connective tissue mass, which contains much elastic tissue and groups of fat cells, and which passes over into the neighboring connective tissue between the external and internal carotid.

From this connective tissue there are numerous projections between the lobules and the glomeruli, forming a net about them.

The same richly cellular masses which Arnold found in the connective tissue of the coccygeal gland are also found here in the connective tissue about the nerves of small vessels. The cells are at times round, at times long and more spindle-shaped, and consist of a very large nucleus containing fat and a narrow border. They are in rows or groups on both sides of the vessel, and in the meshes of the capillaries, and also in those projections of tissue which envelop the lobules and glomeruli, and the fat contained makes them appear not unlike ganglion cells.

The intercarotid body lies in the cellular tissue on the posterior

border of the fork of the common carotid, and is turned more toward the internal carotid, receiving its blood supply from the common carotid.

Low-power microscope shows a compact fibrous capsule which is easily separated from the loose cellular tissue surrounding it, and contains numerous vessels and nerves. From this capsule go off projections of various size, which enter the gland and surround the lobules. These lobules are varied in number and size; for example, if large, only three appear in the greatest cross-section; generally there are only four or five such in the whole organ, while if they are small there may be ten or twelve.

Kartschenko found that the intercarotid body developed from an outgrowth of the adventitia of the carotid, and that a thymus nodule had been mistaken for this intercarotid gland.

Paltauf agrees fully with Kartschenko.

In the human embryo of about 15 mm., in which the thyroid layers were still joined to the pharynx epithelium, Paltauf could find no trace of the carotid gland except a slight thickening of the adventitia of the carotid. He could, however, find no trace of epithelium in the location where the carotid gland would later develop.

In an embryo 4 cm. long the carotid gland had begun to develop at the division of the carotid. It was still surrounded by adventitia and appeared as an ovoid (in cross-section round) body, plainly differentiated from the vessels. It lay in the posterior and somewhat inner part of the external carotid, more or less embedded in its adventitia; it consisted of very cellular connective tissue, and already contained numerous vessels which branched off from proportionately large branches of the external carotid.

Prompt recognition of the existence and relations of the tumor of the intercarotid body will facilitate a complete and immediate removal of the growth, together with the larger vessels.

A STUDY OF THE PHYSICAL SIGNS OF LOBAR PNEUMONIA.[1]

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Among the cases of primary lobar pneumonia admitted to the wards of the Hudson Street Hospital between the years 1896 and 1902 there

[1] Read at a meeting of the New York Society of Internal Medicine, January 21, 1903.

were 392 in which the physical signs could be satisfactorily studied. The records of these 392 cases have been tabulated and analyzed and form the basis of the studies here presented.

With comparatively few exceptions all of these cases, throughout their stay in the hospital, were under the observation and care of one of the writers (Conner). The arrangement of the hospital service—that of having a single attending physician with a continuous service throughout the year—has made it possible to have the records uniform and consistent in so far, at least, as applies to methods of examination, nomenclature, and the interpretation of physical signs.

Throughout this period two points especially in the physical signs have been kept in mind in the hope that a careful observation of the cases in these particulars might eventually aid in clearing up the present uncertainty regarding them. These are, first, the character in the breathing in the early stage of pneumonia, and, second, the physical signs and the frequency of the condition known as "central pneumonia."

Concerning the methods of physical examination used nothing need be said except as to the method employed in auscultation. It has been our custom throughout this series to use the ear itself, rather than the stethoscope, in listening to the chest. We are convinced that the finer shades of breathing can be more readily distinguished by the ear applied directly to the chest than through the intervention of the stethoscope. This latter instrument has been used only in examining the supraclavicular regions and, occasionally, in searching for râles.

It seems proper, perhaps, to offer here a word of caution concerning two possible sources of error in the physical exploration of the chest. To the first of these attention has often been called. Concerning the second we have as yet seen no mention.

1. In the case of forced breathing *through the mouth* a distinctly tubular quality is frequently given to the breath sounds, and especially to the expiratory sound, as heard through the chest. These sounds are occasionally so loud and distinct as to almost mask the vesicular murmur. This difficulty can usually be overcome, of course, by having the patient breathe through the nose.

2. In examining the back of a patient who is lying on his side, the lower side of the chest, because of its compression or, perhaps, because of its contact with the mattress, will give, almost always, a percussion note noticeably deeper and more resonant than that of the upper side. This contrast may be so marked that the upper side will seem to lack resonance and may be looked upon as abnormal. Resistance to the examining finger on percussion, also, is subject to the same variation, and even the breathing sounds are often appreciably altered on the compressed side—there being a faint tubular element added to the

vesicular sounds. These errors can best be avoided by having the patient sit up and lean forward. If the upright position cannot be used he should be examined lying first on one side and then on the other, or else examined lying flat on his face. The objection to the last position is that unless the arms are folded in front the scapulæ are forced backward and made prominent, so that the interscapular space is much narrower, and examination there made difficult.

Character of the Breath Sounds in the Early Stage of Pneumonia. From the frequency of the disease, the ease with which it is recognized, and the definite nature of its onset, it might be supposed that all uncertainty regarding its physical signs had long since disappeared and that there was practically unanimity concerning the manifestation, to physical examination, of its various aspects and stages. Such is, indeed, the case for the signs of complete consolidation and, to a less extent, for the signs of resolution. With the signs of the early stage, however, before consolidation has become complete, the case is quite different. This is made apparent at once by reference to the various authoritative writers upon the subject. Concerning the percussion signs—the impaired resonance (with or without a tympanitic quality), gradually increasing to definite dulness—and the presence of the crepitant râle there is fairly general agreement. As regards the changes in the breath sounds, however, both as to their nature and their diagnostic value, there is still much uncertainty and difference of opinion.

Laennec[1] himself, in his elaborate description of the auscultatory signs of the disease, does not describe at all the nature of the breathing in the early stage, but implies that it is not characteristically changed, by speaking of the crepitant râle as the pathognomonic sign of the first stage. Flint's[2] views are much the same; thus he says: "The physical diagnosis of acute lobar pneumonia in the first stage must be based on the presence of the crepitant râle, with moderate or slight dulness on percussion over the affected lobe. . . . When the crepitant râle is wanting a positive physical diagnosis must be deferred until more or less of the affected lobe becomes consolidated; that is, when the disease passes into the second stage."

The earliest definite statements concerning the character of the breathing in the first stage seem to be those of Stokes[3] and Grisolle. The former says: "The physical signs of the first stage of pneumonia are still to be determined with accuracy. Without possessing a sufficient number of observations to determine the point, I am led to the belief that an intense puerility of respiration in the affected part will

[1] A Treatise on Diseases of the Chest, 1834, 4th Eng. edit., p. 194.
[2] Manual of Auscultation and Percussion, 1885, 4th edit., p. 180.
[3] Diseases of the Chest, New Sydenham edit., p. 282.

be found to be the principal phenomenon." Grisolle,[1] on the other hand, asserts that "in the great majority of cases, if not in all, a diminution in the strength of the respiratory murmur is the first stethoscopic phenomenon that marks the onset of the pneumonia." Referring to Stokes' view concerning the harshness of the breathing, he adds that he has never observed puerile breathing as the first auscultatory sign.

Fuller,[2] writing twenty-five years later, indorses Grisolle's views. "My observations," he writes, "incline me to assert with Grisolle that the weakness of the respiratory murmur attended by loss of purity and softness usually characterizes the beginning of the disease."

Walshe[3] gives his opinion as follows: "The breathing sounds reach the ear weaker, harsher, and rougher, and of higher pitch than natural from the infected part, provided this is near the surface. If the structure involved be deep-seated, on the contrary, exaggerated respiration, from the intervening healthy tissue, is heard."

Wilson Fox's[4] statement is similar, thus: "Sometimes, as was first noticed by Stokes, an increased harshness of the respiratory murmur may be the first phenomenon observed, but this is not constantly present. . . . In some cases the respiratory murmur is weakened and loses in clearness and softness, acquiring almost *ab initio* the character of the 'indeterminate' breathing of Skoda." Juergensen[5] says: "Among the auscultatory signs the crepitant râle ranks first. . . . Before the pneumonia has reached the surface of the lung the breathing which is heard over the part affected is generally different from that heard over the other portions, but the difference is not always of the same character; now it is sharply defined and puerile, now weak, but still clearly vesicular."

Among the recent American writers, Osler,[6] Cabot,[7] and Thompson[8] have noted the frequency with which a diminution in the vesicular murmur is found in the first stage. A. H. Smith[9] does not describe the character of the breathing in the first stage and emphasizes the importance of the crepitant râle. Among the later German writers Strümpell[10] makes no mention of the character of the breathing. Aufrecht[11] declares that Grisolle's statement concerning the feeble

[1] Traité Pratique de la Pneumonie, Paris, 1841, p. 231.
[2] Diseases of the Lungs, London, 1867, 2d edit., p. 258.
[3] Diseases of the Lungs, London, 1871, 4th edit., p. 349.
[4] Diseases of the Lungs and Pleura, London, 1891, p. 297.
[5] Ziemssen's Cyclopædia of the Practice of Medicine, New York, 1875, vol. v. p. 82.
[6] The Principles and Practice of Medicine, New York, 1899. 3d edit., p. 119.
[7] Physical Diagnosis, New York, 1900, p. 240.
[8] Practical Medicine, New York, 1902, 2d edit., p. 174.
[9] Twentieth Century Practice of Medicine, vol. xvi. p. 21.
[10] Lehrb. d. spec. Path. und Therapie, 1899, 12th edit., Bd. i. S. 325.
[11] Nothnagel's spec. Pathol. und Therapie, Bd. xiv. S. 85.

breath sounds in the first stage has received no special indorsement from any direction, and adds that "the crepitant râle remains the characteristic symptom of the inflammatory invasion of the lung."

In many cases, he says, there is also prolongation of the expiratory murmur.

Without continuing the citations, it is evident that with regard to the various opinions held the writers may be grouped under several heads.

1. Those who recognize no significant change in the breathing of the first stage, and who regard the crepitant râle as the only characteristic sign of the beginning pneumonia.

2. Those who believe the breath sounds to be usually abnormally harsh or puerile.

3. Those who find the diminution in strength of the vesicular murmur to be the usual sign.

4. Those who believe the breathing to be appreciably altered in most cases, but who think that it follows no constant rule and may be either diminished or puerile.

Observations in the Present Series of Cases. Among the 392 cases observed there were 129 in which no bronchial breathing was present on admission to the hospital. Of these 5 were cases admitted during resolution. Of the 124 cases admitted early in the disease, in which no bronchial breathing was present at first, there were 98 (79 per cent.) in which the respiratory murmur over the affected area was noticeably *diminished* as compared with that of the other side, or of other parts of the same lung.

In 8 of the remaining 26 cases the murmur was described as "harsh" or "exaggerated vesicular," and in 4 cases as "bronchovesicular." In 14 cases no appreciable change in the breathing was recognized.

In a few cases admitted very early in the disease the enfeeblement of the respiratory murmur was not evident at the first examination, but appeared very soon afterward. The area of changed breathing could usually be outlined quite distinctly from the normal murmur beyond, and usually corresponded fairly with the area of impaired resonance or dulness. The change, in most cases, was one not merely of intensity; there was usually as well a very distinct lessening of the breezy, rustling character—a faint, thin, rather high-pitched sound, which while losing much of the rustling quality of normal breathing had yet acquired no trace of tubular quality, even in its expiratory phase—a murmur not only *feeble* in intensity, but *indistinct* in quality.

In favorable cases it was possible to watch the development and progress of this change in the breathing for a period of two or three days before any sign of bronchial breathing appeared. In these cases a gradual and progressive enfeeblement, and at the same time a

progressive loss of the rustling quality, could be noted until, just before the appearance of tubular breathing, the breath sounds were almost entirely suppressed; and if, as usually happened in such cases, the dulness had become distinct and that portion of the chest immobile or nearly so, the resemblance of the signs to those of moderate amounts of pleuritic effusion was quite marked. As regards the length of the two respiratory acts, usually little change from the normal ratio was observed. At least there was no considerable prolongation of expiration.

Time of the Appearance of Feeble Breathing. This enfeeblement of the breathing must appear very early, usually within twenty-four hours of the onset. Of the 98 cases showing this sign 13 were admitted on the first day of the disease. In 10 of these the first examination showed an area of diminished breathing. In 2 others this appeared upon the second day and in the last case upon the third day of the disease. Twenty-six of the 98 cases were admitted upon the second day of the attack. In all but 1 of these the sign was present on admission. In the last case it appeared the next day. In 1 case the change was appreciable within twelve hours of the initial chill.

Relation of the Appearance of Dulness to that of Indistinct Breathing. Among the 98 cases with indistinct breathing 89 showed the presence of the modified breathing upon the first examination. In most of these there was also appreciable at the first examination more or less distinct impairment of resonance over the same region. In these latter cases it was, of course, impossible to determine which of the two signs had appeared the earlier. In 13 of the 98 cases it could be demonstrated that a localized enfeeblement of the breath sounds existed before any impairment of resonance could be detected. In most of these cases the interval between the recognition of feeble breathing and of diminished resonance was only a few hours. In 2 cases, however, a change on percussion was not recognized until forty-eight hours after the change in breathing had been noted.

On the other hand, in 3 cases some impairment of resonance was found before any change in the vesicular murmur could be detected.

Duration of the Period of Diminished Breathing. The length of time during which an area of feeble breathing was *observed* before the appearance of bronchial breathing varied as follows:

In 48 cases	. . . . .	1 day or less.
" 20 "	. . . . .	2 days.
" 3 "	. . . . .	3 "
" 3 "	. . . . .	4 "
" 3 "	. . . . .	5 "

Since in many of the cases the change in breathing was present at the first examination, it seems probable that these figures represent rather less than the usual duration of the stage of feeble breathing.

Cause of Diminished Breathing. Speculation concerning the physical causes underlying the production of the various pulmonary physical signs is a fascinating but perhaps unremunerative occupation, and we shall not be led into a discussion of these except in the case of the sign now under consideration. In a beginning pneumonia, with engorgement of the capillaries and swelling of the mucous membrane of the bronchioles, one might perhaps, *a priori*, expect the vesicular murmur over the affected area to be loud and harsh. Skoda says: "The greater the opposition produced by contractility to the entrance of air into the air cells, and the more rapid and complete the inspiratory movements, the louder will be the vesicular murmur." Why then should diminished breathing be a feature of so large proportion of beginning pneumonia? Von Basch,[1] some years ago, called attention to the fact that in the passive engorgement of the pulmonary capillaries, which is so frequent a condition in uncompensated cardiac disease, the lungs are very considerably enlarged by the tendency of the tortuous capillaries to straighten out when they are stretched by an increased amount of blood within them. This increase in volume of the lungs he showed is associated with a marked loss of elasticity, and consequently with much restricted respiratory expansion—conditions to which he gave the names "Lungenschwellung" and "Lungenstarrheit." He believes that a part of the dyspnœa in such uncompensated cardiac cases is due to the very limited respiratory movement of the swollen and rigid lungs.

That such a general engorgement of the lung capillaries does produce both swelling and rigidity of the lungs we have seen clearly demonstrated recently in a series of ingenious experiments on animals, kindly undertaken by Professor Hartwell, of the physiological department of the Cornell University Medical College, New York. It seems not unreasonable to assume that these results may with propriety be applied to the local engorgement of a beginning pneumonia, and, if this be true, a satisfactory explanation of the marked enfeeblement of the respiratory murmur is at hand in the greatly restricted expansion of that enlarged and stiffened part of the lung. With the onset of exudation the rigidity and lack of expansion would presumably be increased, and the progressive diminution in the strength of the respiratory murmur would seem thus to be satisfactorily explained. It is possible that in some cases the limited expansion of the involved portion of the lung may depend in part upon the inhibitory effect of pain, but this is certainly not the usual nor the chief cause.

Harsh or Puerile Breathing in the First Stage. As has been said, an area of harsh or exaggerated vesicular breathing was heard in 8 out

[1] Wiener med. Presse, 1888, Bd. xxix. S. 567.

of 124 cases of beginning pneumonia (6½ per cent.). As to its significance at such a time, our views correspond with those of Walshe, who says: "If the structure involved be deep-seated, exaggerated respiration from the intervening healthy tissue is heard."

Râles in the First Stage. Among the 129 cases seen before the advent of bronchial breathing, râles of some sort were heard in 110 (85 per cent.). Of these about 50 per cent. are described as "crepitant." Most of the remainder are called "subcrepitant." Some few are designated "friction sounds."

Ever since the recognition of the crepitant râle by Laennec, and his assertion that its presence was pathognomonic of pneumonia, there has been much difference of opinion not only as to its cause and site, but, as well, as to its frequency and its significance. While few have been willing to take the extreme position of Laennec concerning its diagnostic value, many, and perhaps most, careful clinicians since that time have looked upon it as the chief and characteristic physical sign of the early stage of pneumonia.

Skeptics concerning its importance have not been lacking, however, as may be seen from the following quotation of that master of physical diagnosis, Skoda.[1] He writes: "Andral, Cruveilhier, Chomel, etc., have brought forward numerous facts which prove that Laennec's crepitating râle cannot be regarded as such a sign (pathognomonic of pneumonia), and that in fact no distinctive line can be drawn between crepitating, subcrepitating, and mucous râles. . . . I have not only not found this crepitation constantly present in pneumonia, but, if we are to follow Laennec's description of it very closely, I must say that I have not often observed it."

Our experience in the cases here studied corresponds somewhat closely to the statement just quoted. Although râles were heard in 85 per cent. of all the cases seen before the appearance of the bronchial signs, in only one-half of this number were they classed as crepitant. Under this head were included only fine râles heard during the latter part of inspiration and at no other time. Many of these, however, did not correspond accurately in quality to the dry, crackling sound suggested by the classical comparisons of twisting a lock of hair close to the ear, or of subjecting salt to gentle heat. Variations were found not only in the "fineness" of the sounds, but also in the degree of "dryness" or "moistness," and it was not infrequently difficult to say, with respect to a particular râle, whether it should be classed as crepitant or subcrepitant. On the other hand, râles answering in all essential particulars the description of crepitant râles, we have heard occasionally in conditions in which pneumonia could be easily excluded, especially

[1] Auscultation and Percussion, English translation, 1854, p. 156.

in patients who have maintained dorsal decubitus for some time and in cases of dry pleurisy.

Basing our conclusions, then, on what has already been said, we would place in their order of relative frequency and importance the physical signs of a beginning pneumonia as follows:

1. A circumscribed area of feeble, indistinct breathing as compared with the breathing at a corresponding point on the other side (with the patient, if possible, in a sitting position).

2. A circumscribed area of impaired resonance, with or without a tympanitic quality, obtained under similar precautions.

3. The crepitant râle.

4. A slight increase in the intensity and clearness of the vocal resonance.

Physical Signs of the Second Stage. Whatever may be the physics of the production of bronchial breathing and bronchophony, it will probably not be disputed that the appearance of these signs well developed is coincident with and indicative of complete hepatization of a larger or smaller portion of lung tissue.

It may be well to explain at once that we have used the terms "bronchial" and "tubular," as applied to types of breathing, as synonymous and interchangeable in all respects. It is not uncommon, in this city at least, to find the term "tubular breathing" restricted to the less intense and lower-pitched types of bronchial breathing. On the other hand, with certain of the English writers,[1] this arrangement is just reversed, and "tubular" rather than "bronchial" is the term applied to the intense, high-pitched bronchial breathing typical of the second stage of pneumonia. It has seemed to us, however, that confusion would be less likely to occur if the term bronchial were retained for all grades of breathing characterized by a tubular quality, and if further distinction were made by qualifying it with adjectives expressive of intensity, pitch, distance from the ear, etc.

The development of bronchial breathing in most of the cases studied, while by no means altogether uniform in manner, nevertheless seemed to follow fairly distinct lines. Almost without exception the bronchial quality first appeared with expiration. This fact has, of course, long been recognized, and it is interesting to note that credit for its first recognition is given by Grisolle to the American physician, James Jackson.

In most cases these early expiratory bronchial sounds have been faint, soft, and of very low pitch. The period at the beginning of hepatization during which the bronchial quality was evident only with expiration varied greatly in our cases. Usually it was less than twelve

[1] Pye-Smith. Allbutt's System of Medicine, vol. vi. p. 101.

hours. Occasionally, however, it lasted for twenty-four hours, and in at least two cases it amounted to two days.

The bronchial breathing seemed usually to develop in one of two ways. The more frequent course was for the breath sounds, both inspiratory and expiratory, when first heard to be faint, soft, and of very low pitch. Gradually both sounds would grow louder and harsher and the pitch become higher until the familiar intense, shrill breathing was reached. The second and less common way was for the indistinct, scarcely audible breath sounds of the latter part of the first stage to change quite suddenly into faint but high-pitched bronchial breathing; the bronchial expiration preceding by only a very few hours, if at all, the bronchial inspiration. These faint sounds would gradually become loud and harsh, the pitch meantime showing no appreciable change. The bronchial signs, at first heard over a very small spot, would gradually extend over the neighboring areas which until then had belonged to the curious "silent region" that we have come to regard as so characteristic of incomplete consolidation.

Concerning the signs of percussion in the second stage, only one point will be mentioned. When the consolidation affects, as it so frequently does, the right lower lobe posteriorly, there is found very commonly over the middle lobe in front a strikingly deep, hyperresonant note of more or less distinctly tympanitic quality. This note is heard usually over quite a circumscribed area in the fourth and fifth spaces within the nipple line. It is, of course, a familiar experience to encounter such a hyperresonant note wherever the lung tension is relaxed near a consolidated area or above fluid. This is peculiar only in that it is so frequently heard in just that particular spot rather than over regions nearer the seat of consolidation, where it might perhaps more naturally be expected. This sign has been so frequently found among these cases that in examining the front of the chest in a patient suspected of having pneumonia, it has often been possible by it to predict the position of the consolidation before the back had been examined.

Day of Appearance of Bronchial Breathing. Among the cases in which bronchial breathing and bronchophony appeared after admission to the hospital, the relation of its appearance to the day of the disease was as follows:

1st day	2 cases.	6th day	9 cases.
2d "	14 "	7th "	3 "
3d "	19 "	8th "	5 "
4th "	30 "	11th "	1 case.
5th "	15 "		

It should be borne in mind that this table necessarily gives undue prominence to the cases in which the signs of consolidation appeared late, since those cases are, of course, the ones most likely to develop their signs in the hospital.

In four cases of undoubted pneumonia, neither bronchial breathing nor bronchophony could be found at any time.

Concerning the relation of bronchophony to bronchial breathing, it may be said that usually its appearance and disappearance were found to correspond closely to those of bronchial breathing, although not infrequently it was a little later in appearing and a little earlier in disappearing. In a very few cases it was heard very slightly in advance of bronchial breathing.

Massive Pneumonia. No instance of this rare form of pneumonia was found among the forty autopsies of this series, nor were the physical signs in any of the cases observed such as to suggest that the bronchi as well as the alveoli were plugged with fibrinous exudate.

Signs of the Stage of Resolution. The gradations of change from bronchial to normal vesicular breathing progressed usually in a definite inverse order to that observed in the development of the consolidation —that is to say, the intense, high-pitched bronchial inspiratory and expiratory sounds became step by step lower pitched, softer, and fainter. Then the bronchial quality of the inspiratory sound disappeared altogether and finally the bronchial expiratory sound was lost. In one particular, however, the signs of resolution differed from those of beginning consolidation. The stage of feeble breathing, which was present in so large a proportion of the cases in the early stage, was found much less frequently during resolution. In a majority of cases the soft, low bronchial breathing merged directly into a harsh vesicular murmur. In a few cases, however, the stage of feeble breathing was not only present, but was very marked and was prolonged for two or three days. In these cases almost no râles were heard and the signs somewhat suggested pleuritic effusion.

Relation of the Disappearance of Bronchial Breathing to Defervescence. In 199 uncomplicated cases in which this relation could be determined, the results were as follows:

Disappearance of bronchial signs before defervescence	39 times.	20 per ct.
On day of defervescence	25 "	12 "
One day after defervescence	28 "	14 "
Two days " "	19 "	9 "
Three days after "	22 "	11½ "
Four days " "	22 "	11½ "
Five days " "	14 "	7 "
Six days " "	7 "	3½ "
Seven days " "	3 "	1½ "
More than seven days after defervescence	20 "	10 "

In studying these cases at the bedside, with respect to the relation of the time of resolution to that of defervescence, they have seemed to fall into three fairly distinct groups:

1. Those in which the signs of consolidation disappeared one, two, or even three days before the temperature fell. In these cases, in spite of

the fact that bronchial breathing, bronchophony, and most of the dulness had disappeared, and that the vesicular character of the murmur showed that the air was entering the alveoli, no fall in temperature and no special improvement would occur for thirty-six, forty-eight, or even seventy-two hours. Then, however, in many cases, the temperature would fall to normal as abruptly and the crisis be as distinct as in ordinary cases.

2. Those cases, by far the greatest in number, in which beginning resolution coincided with the fall in temperature, or followed it within a day or two, and in which resolution progressed rapidly and was complete within a very few days more.

3. Those cases in which, with a defervescence at the usual time, the signs of complete consolidation persisted for several days or longer before any evidence of beginning resolution appeared.

It is a matter purely of arbitrary arrangement whether all these last cases should be classed as instances of delayed resolution, or whether that term should be reserved for the cases in which the signs of consolidation persisted for a considerable period (say a week or more) beyond the usual time of defervescence. The clinical picture in all the cases was much the same. A temperature normal or nearly so, persistent dulness, bronchophony, high-pitched bronchial breathing day by day becoming softer and lower pitched, and an almost complete absence of the râle redux. This absence of râles was a noticeable feature of almost all the cases and presented a striking contrast to the cases of the first two groups in which the râles of resolution were usually very abundant.

Bronchovesicular Breathing. We have intentionally avoided the use of the term bronchovesicular breathing because it is apt to convey to different minds such very different meanings. If one adheres strictly to Flint's description of it as a type of breathing in which the inspiratory phase is composed of two elements—vesicular and bronchial—while the expiration is prolonged, high-pitched, and tubular, we must admit that the sound has been rather infrequently heard by us. If, however, the name be applied to the type of breathing in which the inspiratory sound is vesicular and the expiratory bronchial, then we would say that bronchovesicular breathing had been heard in almost every one of all the cases studied, both at the beginning and at the end of consolidation.

Delayed Resolution. Including under this head only cases in which the signs of consolidation lasted for more than two weeks, there were thirty such. Among these were fifteen cases in which the signs of consolidation lasted between fifteen and twenty days, nine cases in which they lasted between twenty and thirty days, five cases between thirty and forty days, and one case which showed signs of consolidation for sixty days.

In these cases defervescence occurred by crisis fifteen times, by lysis of not more than four or five days, eleven times; and in the remaining four cases some irregular temperature lasted throughout the whole period of consolidation. In none of these cases of delayed resolution were the râles abundant, and in most cases they were almost entirely lacking.

A very interesting and curious feature in two of the cases was the appearance of loud, pure, amphoric breathing, which lasted for a number of days. In one case the right lower lobe posteriorly was involved; in the other the whole of the left upper lobe. In this latter case there was also present for several days, over the lower half of the lobe anteriorly, a clear tympanitic percussion note and a lessened sense of resistance to the finger, so that the signs presented an extraordinary likeness to those of pneumothorax. It seemed probable that the tympanitic note was the transmitted tympany of the adjacent distended stomach. It would be interesting to know if this same proximity of the stomach could explain the conversion of bronchial into amphoric breathing.

Central Pneumonia. This obscure condition is referred to by almost all writers on the subject of pneumonia, but it is difficult to obtain from the descriptions a definite idea either of its frequency or of its physical signs. It is a common habit to apply this term to all cases in which the signs of consolidation are late in appearing. This we believe to be entirely unwarranted. It was by no means uncommon to find in the cases of this series a period of from two to four days in which the only physical signs of pneumonia were a somewhat impaired percussion note over the affected area and very much diminished breath-sounds, and yet these were assuredly not all cases of central consolidation.

There is much clinical and *post-mortem* evidence to show that this stage of diminished breathing in pneumonia corresponds with a condition of *incomplete* consolidation (or marked engorgement) of a considerable portion of lung tissue rather than with a small area of *complete* consolidation in the interior of the lobe and fairly normal tissue at the periphery. On the other hand, there is also much evidence to show that bronchial breathing is a characteristic sign of complete consolidation, whether deep in the interior of the lung or at the surface, provided that the area be large enough to include in it a bronchus of fair size. When the consolidation is deep in the lung such bronchial breathing lacks, of course, the intensity and the sense of nearness to the ear which is so characteristic of consolidation at the surface. Its quality, however, is none the less tubular for its being distant. If now the tissue at the periphery over such an area of consolidation be unaffected, we should expect, and we do get, a vesicular murmur at

the same time with the tubular sounds. In other words, there is heard with each of the two respiratory acts two distinct sounds, a distant bronchial sound and a superficial vesicular one—true bronchovesicular breathing. An opportunity to study a condition analogous to that of central pneumonia is often offered in cases of pneumonia of the upper lobe, in which the consolidation affects at first only the posterior portion. Behind there is heard shrill bronchial breathing and dulness, while percussion over the lobe in front, in such cases, gives a deep hyperresonant or tympanitic note, and auscultation shows a puerile vesicular murmur, through which can be readily recognized the distant bronchial sounds, both inspiratory and expiratory, transmitted from the consolidated area behind.

As the process extends and the anterior portion shows first engorgement and then incomplete consolidation, the harsh vesicular element becomes fainter and less distinct, the bronchial element at the same time being more easily heard, but still somewhat distant. Finally, when complete consolidation develops in front, the bronchial breathing assumes the familiar loud, shrill character.

One frequently hears, and sometimes reads, the statement that at a certain time and at a certain place on the chest wall the "consolidation reached the surface," meaning that at that time or place signs of consolidation were first noticed. The idea conveyed is, of course, that consolidation existed before somewhere beneath the surface and had gradually extended to the surface, and that it disclosed itself by physical signs only when the periphery of the lung was reached. Such a view we believe to be entirely at variance with the facts of pathology and with the theory of the production of physical signs. As we have tried to show above, complete hepatization of any considerable extent presents characteristic auscultatory signs, whether it be in the interior of the lung or at the surface; whereas incomplete consolidation, no matter how extensive in area or how close to the surface, fails to show such bronchial breathing. When, then, bronchial breathing and bronchophony are heard at some point over a lobe where previously no such signs existed, they signify not that a deep area of hepatization has extended to the surface, but that an area of incomplete consolidation has, at some point opposite the ear, become complete.

Among this series of cases there were but four in which the course and sequence of the physical signs made it altogether clear that the condition was one of a central consolidation which gradually extended to the surface. The physical signs in all these cases were very similar and consisted, in each case, at first of an area of somewhat exaggerated vesicular breathing and a hyperresonant percussion note with no râles. Later, through the vesicular breathing faint, distant bronchial breathing could be heard, although no impairment of resonance was apparent.

Later still the vesicular murmur became less distinct and loud, while the bronchial breathing grew louder and nearer. Finally, well-marked dulness developed and bronchial breathing and bronchophony became shrill and intense.

Without venturing an opinion as to the absolute frequency of cases of central pneumonia, we nevertheless believe them to be much rarer than is popularly supposed, and we believe also that the comparatively frequent cases of marked delay in the appearance of the signs of consolidation are cases not of a centrally situated consolidation slowly working to the surface, but rather cases of very slow progress from engorgement to complete hepatization.

Pitch of Bronchial Breathing. In following closely the changes occurring in bronchial breathing from the time of its appearance to its disappearance, one is impressed, in most cases, with the very marked variation that occurs in the pitch. These changes are especially easy to observe where the consolidation is slow in developing, and it is in such cases also that the greatest range of pitch is seen. As has been said, the first bronchial sound recognized is with expiration. Beginning as a hollow, soft, low-pitched sound, the pitch is steadily raised and the intensity increased until the characteristic shrill, high sound is reached. There, as resolution begins, the process is reversed and the pitch falls and the intensity diminishes until nothing but the same soft, low-pitched bronchial expiration remains. We have come to believe that this progressive rise and fall in the pitch is related rather to the degree of consolidation than to the proximity of the consolidation to the surface. In the very rapidly forming consolidations the stage of low pitch is often not seen at all, whereas, as has been said, it is in the very slowly forming hepatizations that the progressive rise and fall in pitch and intensity are most evident.

PRIMARY CARCINOMA OF THE LIVER.

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The association of carcinoma, adenoma, and cirrhosis, which is the usual rule in primary carcinoma of the liver, brings into prominence the relationship of chronic inflammation and the development of both benign and malignant neoplasms, at the same time as it emphasizes the close relation of the two types of neoplasm. Therefore, all such cases have a peculiar interest for the study of the etiological factors in tumor formation, in addition to the interest they possess as representing one

of the rarest forms of primary carcinoma. This report has to do with a typical instance of primary carcinoma of the liver associated with advanced atrophic cirrhosis and adenoma formation. Of special interest are the facts that the tumor was latent, the patient dying from uræmia before the growth had caused appreciable trouble; that the cirrhosis had existed longer than is ordinarily the case, because collateral circulation had relieved the ascites that had once existed, the new vessels of old perityphlitic adhesions having become distended to a high degree. There are also certain points in the minute anatomy that seem of importance in explaining the manner of formation of primary liver carcinoma.

Eggel's[1] comprehensive review of this subject has appeared so recently that any further search in the literature is unnecessary except to record the few cases reported since that time. In early reports the use of the term "adenoma" and "carcinoma" has been peculiarly loose when applied to growths in the liver, there having been a marked tendency to designate as adenoma all epithelial growths that did not produce metastases or infiltrate the liver substance in a characteristically malignant fashion. The French writers have been especially inclined to do this, and they have also included as adenomas many instances in which there were metastases. Another source of error is in incomplete search for obscure primary growths. Eggel has included in his tables only such tumors as showed metastases or infiltration of malignant character, or those that, lacking these features, presented microscopic evidences of malignancy. The microscopic evidences consisted of atypical structure, abundant karyokinesis that is often multipolar or asymmetrical, giant cells, and infiltration of the tumor cells into the normal tissues and vessels. As a rule, it is not hard to distinguish the adenomas. Often they consist practically of normal liver tissue encapsulated in a nodule, although generally there are more variations from the normal, of which hypertrophied cells, tubular formations, and tangled cords are common. Adenomas derived from bile vessels more closely resemble carcinoma. Considering the above-mentioned requirements Eggel collects from the literature 163 cases, which he tabulates, as well as five or six more that are described in an *addendum*, having escaped his first collection or being of more recent date.

Two types are distinguished by their microscopic characters as *carcinoma solidum* and *carcinoma adenomatosum*. Upon a macroscopic basis are separated the (*a*) nodular, (*b*) massive or solid, and (*c*) diffuse forms. Primary carcinoma of the liver can originate from the cells of the smaller bile ducts or from the liver cells themselves. Formerly there were included many cases of carcinoma arising in the larger bile

[1] Ziegler's Beiträge, 1901, vol. xxx. p. 506,

ducts, or even in the gall-bladder, and the exclusion of all these explains the discrepancy of Eggel's statistics when compared with those of earlier writers. He finds that carcinoma of the liver constitutes about 2.65 per cent. of all fatal ailments that come to autopsy, and that about 2.3 per cent. of them are primary; this makes primary carcinoma of the liver appear to occur in about one in each 2000 autopsies. Of the 163 tabulated cases there are 117 that are described microscopically, the inclusion of the other 46 being warranted by the macroscopic and clinical findings. From the tables it appears that the proportion of liver-cell carcinoma is far greater than that of bile-duct carcinoma, there being 99 cases of the former and but 17 of the latter. As the author states, this may be because the liver-cell carcinomas have attracted more attention, and have, therefore, been more frequently published. The division into *carcinoma solidum* and *carcinoma adenomatosum* is readily applicable to all microscopically studied cases, of which 62 are solid and 55 adenomatous. The "*carcinoma cylindro-cellulare* of the biliary ducts" of the French writers is, of course, equivalent to *carcinoma adenomatosum* of the biliary ducts. Owing to the multipolar structure of the hepatic cells a cylindro-epithelial carcinoma cannot conceivably arise from them.

Macroscopically considered, the nodular form is the most frequent, 104, or 64.6 per cent., being of this type. The massive form is much less common, there being 37 cases, or 23 per cent.; and still less often occurs the diffuse form, with 20 cases, or 12.4 per cent. The diffuse form was found relatively most frequent among the *carcinoma adenomatosum*, while it was not found at all among those arising from bile-duct epithelium. Moreover, the diffuse form seems to be always primary, for the secondary growths do not take this form, as might be expected; however, Eggel does not agree with those who think that the massive form is also always primary, for the literature contains authentic records of secondary growths that were of this type. While the liver generally is enlarged, even to a weight of 14,000 grammes, it is often kept down by the accompanying atrophic cirrhosis, so that in seven the weight was practically normal, and in eleven it was less than normal. The right lobe was in almost every case the exclusive or at least the principal seat of the new growth, although there were a few cases in which the left was most affected. In the diffuse form the entire liver was always evenly involved, except in Eggel's own case, in which part of the right lobe was still unaffected.

The importance of cirrhosis in primary carcinoma of the liver is brought out well by the figures. Of the eighty-two authors who considered this point, all but twelve noted cirrhosis; that is, 85.4 per cent. of the livers were cirrhotic. The proportions vary somewhat with the different types: In carcinoma of the hepatic cells alone, the cirrhosis

was present in 86.4 per cent.; in those of bile-duct origin, 62.5 per cent.; diffuse form, 75 per cent.; massive form, 90.9 per cent.; nodular, 79 per cent. The cirrhosis itself was atrophic in 88.6 per cent.

It was formerly held that metastases were rare in primary liver carcinoma; but this is incorrect. In 66 per cent. there were secondary growths in other organs, the thoracic and mesenteric glands being most often involved, and next to these the lungs. A marked tendency to grow into large vessels and to cause tumor-thrombi is seen, and even in those cases without metastases in a large part (thirty-five) this condition was found.

Histologically there is no difficulty in recognizing the tumor cells, whether of biliary or hepatic origin. In some cases which were certainly malignant, as shown by metastases, the cells, even in the secondary growths, resembled the normal closely, even to the extent of secreting bile.

Liver carcinoma closely agrees with other forms as regards the age at which it occurs, being most frequent between fifty and sixty, then sixty and seventy, and then between forty and fifty years. A few cases in individuals under twenty years of age have been reported. Agreeing in part with the occurrence of cirrhosis, 63.3 per cent of the collected cases were men. Except for cirrhosis, nothing of importance concerning etiology has been brought out; there are the usual scattering instances of heredity, trauma, etc.

One hundred and forty-seven cases were reported clinically. Usually the first symptoms come from the digestive canal, with loss of appetite, sensations of pressure and fulness, and later diarrhœa or constipation. The amount of pain in the region of the liver seems to vary with the amount of involvement. Icterus occurred in 61 per cent., most often in the diffuse form; ascites in 58.5 per cent.; œdema in 41 per cent.; enlarged spleen in 32 per cent; and fever in but 14 per cent. The duration was found to be very variable, necessarily, since the onset is dated from the first symptoms, after which the average time left was about six months.

Among the articles published on this subject there is a great amount of speculation as to whether the carcinomas originate in the hepatic cells proper, or in the bile ducts, or in both, there being advocates of each view. Eggel takes the position that the carcinoma may originate in either the hepatic or the biliary epithelium, each type showing characteristics of its origin. He opposes the attitude of those who discredit the formation of carcinoma from liver cells on the ground that these cells are too highly specialized to form tumors, by citing instances of the formation of bile by the metastases of these tumors, the production of adenomas from liver cells, and the identity of the structure of the cells of certain tumors with that of liver cells. There can be no ques-

tion that tumors arise from the intrahepatic bile ducts as well as from the same ducts outside of the liver. Ribbert's hypothesis of the genesis of cancer in epithelium removed from its normal environment by inflammatory processes seems to receive the most support in carcinoma of the liver. The cirrhotic process is so frequent in these cases that it seems certain that it must play a part in starting the growth, and there are frequently produced ideal examples of such isolation of epithelium. Cirrhosis seems to be the primary change in most cases, and probably acts by causing proliferation of the epithelium which in rare cases continues to malignancy, perhaps when the cells are placed in peculiar circumstances, as suggested by Ribbert.

Since Eggel's paper was prepared several other cases have been reported which do not in any degree modify his results, but may be briefly mentioned to complete the bibliography. Most sumptuously illustrated is the report published by Catherine H. Travis.[1] The report concerns a colored man, aged forty years, with enlarged, nodular liver, ascites, but no jaundice, suffering with gastric disturbances and pain in the region of the liver. Death occured nine months after the first symptoms began. The liver weighed 3580 grammes, and showed a large growth in the right lobe with many smaller nodules scattered through both lobes, invasion of the portal and hepatic veins, and metastatic growths in the pulmonary arteries and the lungs. There was marked atrophic cirrhosis. Nothing like adenomas is mentioned, so they probably were not present. Histologically the tumor was composed of cells undoubtedly derived from the hepatic epithelium, transitions from the liver cords to tumor cells being described. The pulmonary growths were similar to the parent tumor in character. As to histogenesis, Travis *considers the transition of cell cords in the neighborhood of areas of new-growth into tumor strands the fundamental process*,[2] and describes it as follows: "The cells in the surrounding cords become larger, their nuclei are also enlarged and take a dark hæmatoxylin stain, and this widened atypical strand becomes still wider, comes to have several cells abreast, and passes thus gradually over into one of the cords definitely belonging to the tumor. Proliferation of the tumor cords thus produced can readily be conceived to give rise to nodules of larger and smaller dimensions as they are found all through the left lobe. Through anastomoses of adjacent cords the more complicated variety of the new-growth may arise, as suggested above. The blood capillaries of the liver are evidently continuous with the spaces between the different tumor strands. *The manifold small nodules scattered through the liver are not of metastatic origin, but are primary growths derived by a direct transformation from the liver cells.*"[3] She concludes that "the malignant tumor

[1] Bulletin of the Johns Hopkins Hospital, 1902, vol. xiii. p. 108.
[2] Italics mine.
[3] Italics mine.

possibly results from the progressive atypical growth of hyperplastic masses produced coincidently with the cirrhosis by a reparatory and regenerative process, after the extensive destruction of the liver by some unknown poisonous agent."

In the *Centralblatt f. allg. Pathologie*, 1902, xiii., 327–331, are collected a number of cases recently reported in Italy. D'Alloco[1] reports four cases, the anatomical and histological findings of which can be summarized collectively as follows: Liver in all enlarged, with numerous nodules of different sizes, except in one with a single mass. These nodules corresponded to atypical adenomas of different types, up to true malignant tumors. They were sharply differentiated from the remainder of the liver, which showed only cirrhosis. The author considers that there is necessary for the production of such neoplasms not only an injury by alcohol or similarly, leading to proliferation of the parenchyma and the connective tissue, but also a predisposition of the individual to tumor formation.

G. Jona[2] describes five tumors of the liver, in four of which the origin was in the liver cells, in the fifth from the epithelium of the bile canals. One was a true tubular adenoma, two others were adenocarcinomas with cubic cylindrical epithelium, one an intermediary form between the trabecular epitheliomas and the alveolar carcinomas, and one an alveolar carcinoma. In all cases there was advanced typical atrophic cirrhosis. He concludes that in all the cirrhosis is primary and the carcinoma an episode in its development. Characteristic atypical alterations of the liver parenchyma precede and predispose to the formation of the tumor.

A. Zinno[3] also describes five cases illustrating the gradation from simple adenoma to the most complex form of carcinoma. He thinks that the origin is always in the bile capillaries, which have proliferated subsequent to cirrhosis.

De Vecchi and Guerrini[4] report two cases that they consider sarcoma, associated with cirrhosis.

An additional source of primary tumors of the liver is furnished by the case of primary adrenal tumor, apparently arising in an adrenal rest in the liver, described by Albert Pepere.[5] Here the growth entirely replaced the left lobe, and there were metastases into the right lobe, the entire liver weighing 4650 grammes. Secondary growths also developed in the diaphragm, lungs, and inguinal glands. The gross and microscopic appearances were the same as in renal hypernephroma.

Acland and Dudgeon[6] report a case occurring in a fifteen-year-old

[1] Arch. ital. di med. interna, 1901, Fasc. 1, 2.
[2] Riv. venet. di sc. med., 1900, Fasc. 10.
[3] Giorn. Assoc. med. e natur. Napoli, 1901, Fasc. 5.
[4] Riforma med., 1901, vol. i., Nos. 30–32.
[5] Arch. de méd. exper., 1902, vol. xiv. p. 765.
[6] Lancet, 1902, vol. clxiii. p. 1310.

boy, who shortly before his illness had received on different occasions three heavy blows in the region of the liver. The duration was, so far as clinical indications showed, but about four months, and there was considerable pyrexia and icterus. The liver was enormously enlarged, consisting chiefly of tumor tissue, but there was no cirrhosis. Metastases were abundant. Histologically the tumor is described as a "spheroidal-celled carcinoma arising from hepatic cells." The authors collected from the literature nine cases of carcinoma of the liver in children under twenty years of age, not all of which are unquestionable. To their list should be added a case reported by Bonome,[1] in which an adeno-cancro-cirrhosis was found in an eleven-year-old boy.

The case which I wish to report occurred in a patient at the Norwegian Tabitha Hospital of Chicago, in the service of Dr. Sanberg, upon the body of which autopsy was performed September 3, 1901.

The patient was a man, aged about seventy years. He had always been a heavy drinker, especially when a young man, when he had consumed large amounts of cognac. In middle life he had what appears to have been an attack of appendicitis, followed by the formation of a large abscess in the groin that ruptured spontaneously, and after discharging for a long period eventually healed entirely, leaving a large scar. No history of other sickness, including venereal disease, was obtained.

About six years before his death he had been a patient in the same hospital with a well-marked case of atrophic cirrhosis, characterized principally by ascites, which is said to have been very great. He was treated in the hospital for several months, the ascites gradually disappearing until he was practically well. During the period elapsing until his readmission to the hospital six months before death, he had absolutely no return of the ascites, although his general health had not been good. On his return to the hospital he was free from ascites, and remained so until death, although there was considerable œdema of the subcutaneus tissues, and eventually of the lungs. At this time his symptoms were those of a chronic intoxication, with slight jaundice, xerosis, and pruritus, and the urine contained much albumin and casts. Toward the last a slight fever developed, hearing was lost, and death occurred in coma. It was impossible to say how much of the symptoms was referable to hepatic insufficiency and how much to the nephritis, although it is probable that death was from a true uræmia. Autopsy was performed a few hours after death, while the body was still warm. The report is, in brief, as follows:

External Appearances. The body is that of a large, obese old man; rigor mortis is marked and the conjunctivæ show slight icteric discoloration. The lower limbs, external genitalia, abdomen, and lower part of the thorax show marked œdema. Posterior lividity is marked. The skin over the entire body is covered with dry, branny scales. Over the right half of the fold formed by the pendulous abdomen a large scar is found, forming a deep crease running from the crest of the ilium toward the median line below the umbilicus.

[1] R. instit. veneto di sc. lett. e arti. Resoconti, 1901.

Abdominal Cavity. The subcutaneous fat in the abdominal wall is 3 cm. in thickness, and the muscles are quite pale. There is an umbilical hernia, the sac of which admits the little finger. Both femoral and inguinal rings are closed. The cavity contains but little more than the normal amount of fluid, and the peritoneum is normal. The omentum lies mostly on the right side and is adherent to the parietal peritoneum at the site of the scar noted on external examination; it contains much fat, and a large number of veins which are greatly dilated, some of them being 3 mm. in diameter, so that they form a conspicuous feature. The appendix lies external to the cæcum, passes downward, and the tip is firmly adherent to the scar tissue in the anterior abdominal wall opposite the pelvic brim near the anterior spine. There are a few adhesions between the ascending colon and the abdominal wall; the spleen and gall-bladder are bound to the colon by a few fibrous adhesions.

Both *pleural* cavities and the *pericardial* cavity are free from adhesions, the surfaces are smooth, and there is no excess of fluid.

The mouth and the organs of the neck are normal. There is a slight distention of the veins at the lower end of the œsophagus.

Lungs. The right lung is heavy, especially the lower lobe. The pleural surface is smooth, with the exception of occasional yellowish, pinhead-sized fibrous nodules, apparently healed tubercles. The lung crepitates throughout, but only feebly in the lower lobe. On the cut surface a large amount of frothy fluid exudes from the bronchi and alveoli. The right lung contains no areas of consolidation. The left lung corresponds to the right with the exception that there is a scar in the pleura over the apex.

Heart. The heart is somewhat enlarged, due mostly to thickening of the wall of the left ventricle; it is in systole. The valves, endocardium, and orifices are practically normal. The myocardium shows an increase in the fibrous tissue; there is some sclerosis of the coronary arteries. The aorta shows much atheroma, especially the ascending part; upon some of the atheromatous patches there is a fibrinous deposit.

Liver. The general form is normal, but there has been a great decrease in all dimensions, the measurements being 21 x 13 x 11 x 11 x 5 cm. The entire surface is roughened by both coarse and fine irregularities; most of these are but a few millimetres in diameter, but there are some of a color more like that of normal liver than the rest, that are from 1 to 2 centimetres in diameter. These larger nodules are softer than the rest of the organ, being of about the consistence of normal liver tissue, while the organ as a whole is very hard. The smaller granulations are pale, and the liver as a whole is light yellow in color. There is a distinct bulging of the anterior surface of the right lobe, where there is a certain tenseness as of something within the organ that is soft but under compression. The organ is very firm and elastic, and cuts with greatly increased resistance. The cut surface shows a uniform and great increase in translucent appearing connective tissue, which often replaces the liver substance in considerable areas. The liver tissue that remains bulges on the cut surface as pale yellowish elevations, consisting of one or several lobules. The softer nodules described on the surface are found to be of lenticular form, and they seem to consist of more nearly normal tissue, isolated from the cirrhotic

portions by a thin zone of connective tissue. In the exact centre of the right lobe there is an area in marked contrast to the surrounding liver tissue, from which it bulges slightly, as if released from considerable tension. It consists of a mass of soft, pale tissue, with a few areas of hemorrhage and pultaceous softening in the centre. It is of ellipsoid form, measuring 5 x 4 x 4 cm. The connective tissue about it is very dense, and the few islands of liver tissue are flattened out as if by

FIG. 1.

Section of the liver, showing in the right lobe the encapsulated tumor nodule. The cirrhotic deformity is well shown, and less clearly the secondary growths in the vicinity of the large tumor mass.

pressure from this growth. Its nearest approach to the surface is about 1 cm. from the anterior surface. In the immediate vicinity of this large growth are many smaller nodules of similar appearance, which are distributed with a quite regularly decreasing frequence, going away from the main mass, but there are none so far away as the left lobe. In the hilum of the liver there is a soft, pale mass partly filling the portal vein, which could not be followed in the vessel beyond the hilum. Inside the liver the branch of the portal vein going to the

right lobe is completely filled, but that going to the left is empty. No growths were seen in the hepatic veins.

The gall-bladder is greatly distended with greenish bile, and contains a large number of dark green calculi, but its walls are perfectly normal, as also are the ducts.

Spleen. Adherent to the abdominal wall and to the colon; it is firm, elastic, and greatly enlarged. The capsule is greatly thickened and very tense. On the cut surface the spleen is dark and shows considerable increase of fibrous tissue.

Kidneys. Show an advanced stage of chronic interstitial nephritis, the cortex measuring but about 1 mm. in thickness.

The *alimentary tract* shows a moderate degree of congestion, with follicular enlargement in the colon, but no further change. There was a marked chronic gastritis.

All the other organs were practically normal. Every possible site for a primary tumor growth was carefully investigated, in order to make certain that the growth in the liver was not secondary, but no other growths, either primary or secondary, could be found outside the liver. The glands of the hilum of the liver, as well as those of the thoracic cavity and retroperitoneal tissues were all free from tumor growth or other changes. The mesenteric glands were slightly enlarged, but this was found microscopically to be a simple hyperplasia.

Histological study of the various organs other than the liver brought out nothing that was not disclosed at the autopsy. The summary is as follows:

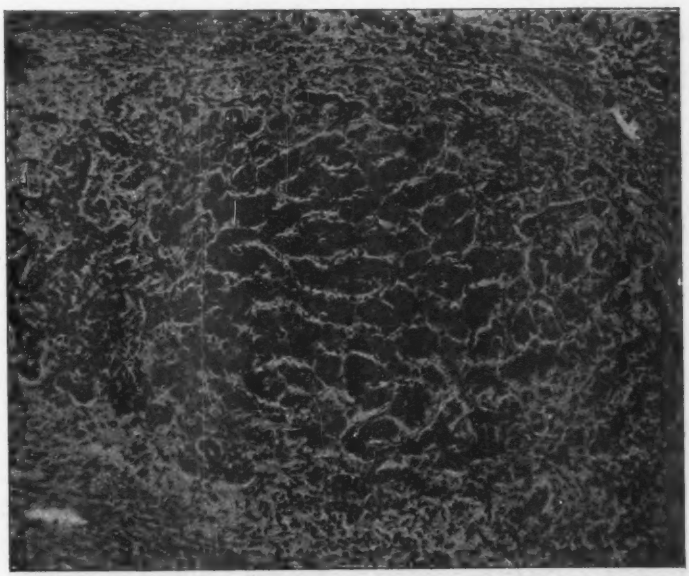
Anatomical Diagnosis. Advanced atrophic cirrhosis of the liver. Primary carcinoma of the right lobe of the liver, with intrahepatic secondary growths, and tumor thrombosis of the portal vein. Multiple hepatic adenomas. Passive congestion of the alimentary tract, spleen, and kidneys. Chronic interstitial nephritis. Pulmonary œdema. Hypertrophy of the left ventricle, and fibrous myocarditis. General arteriosclerosis. Healed suppurative appendicitis, fibrous perityphlitis, with compensatory circulation through the adhesions. Fibrous perisplenitis and pericholecystitis. Umbilical hernia. Healed miliary tuberculosis of the pleura. Icterus (slight) and xerosis. Subcutaneous œdema. Chronic gastritis.

Histological examination of the liver, where not involved in the tumor growths, shows a simple sort of atrophic cirrhosis. There is a large amount of fibrous tissue about each lobule, and in many places foci of round cells are present in this scar tissue. Occasionally individual lobules have been compressed and reduced to a small size, but as a whole the process is multilobular, each island being formed of about half a dozen lobules, between which there is often no connective tissue at all. There is a slight but not great increase in the number of bile ducts in the scar tissue. Some lobules show a slight central congestion, but the liver tissue is, on the whole, remarkably near normal; there is very little fatty infiltration. Not infrequently are found areas in which there are a great many liver columns with cells of unusually large size, and also abundant giant nuclei. Sometimes the greater part of a lobule is made up of such hypertrophied cells, but they are more often limited to the peripheral cords. Not infrequently there are found within the capsule of the lobule, seemingly continuous with the liver-cell cords, columns of oval cells consisting chiefly of nuclear

material, and in no way different from the new bile vessels that lie in the fibrous tissue (Fig. 2); this formation is not marked except in the vicinity of the tumor, and it will be further considered in connection with the histogenesis of the growth.

The small encapsulated nodules that resembled adenomas are found to be but little more than islands of liver tissue that have been less affected by the cirrhosis than the rest of the organ, so that they have been made to bulge when the cirrhotic portions contracted. There may be slightly greater evidences of compensatory proliferation on the part of the liver cells in the shape of hypertrophied cells and nuclei than in

FIG. 2.



An isolated, atrophied liver lobule near the primary tumor, surrounded by connective tissue. Around the edge the proliferation of cells, resembling new-formed bile ducts, is prominent; it is from such individual lobules with marginal proliferation that the tumor nodules seem to arise.

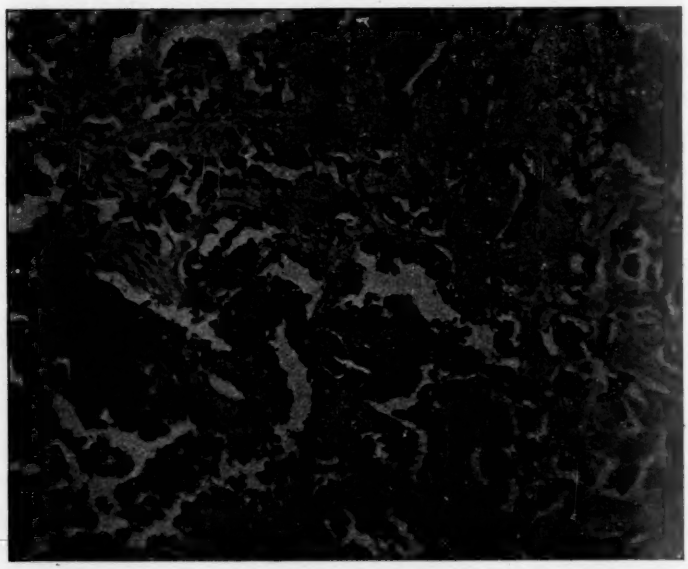
the rest of the liver; but it is not decided. There is no real basis for calling such nodules adenomas, for they are nothing more than the result of a circumscribing proliferative inflammation of the connective tissue, but this has been commonly done. Perhaps the chief reason for this is the occasional occurrence of just such encapsulated nodules in livers that are not cirrhotic. They are very different from the true liver adenomas that consist of atypical formations of bile vessels or liver cords.

The structure of the tumor itself is so complicated that it is impossible to make a simple objective description carry any picture of the growth. There seem to be several different stages in the growth, all

of which occur within a small area, which taken together are confusing, but analyzed seem to show a very definite and interesting series of processes. I may therefore be pardoned for abandoning the objective method to describe the growth by a synthetic process. As can be seen in the photograph of the tumor, a strip was taken from the centre of the main growth out into the sound tissue, and this was reconstructed after sectioning to permit of study of the manner of development. Of course many other portions have been studied.

The most striking fact observed about this growth is that extension does not occur by a simple invasion of the liver tissue by centrifugal growth of the primary mass, as occurs with secondary tumor nodules in the liver. It appears that *the cirrhotic liver nodules that lie just about*

FIG. 3.



Section from centre of a secondary nodule, showing the coexistence of columns of cells, some of which are of the liver-cell type, in masses and columns, and some distinctly like the new-formed bile capillaries. It is possible often to find the two types of cells continuous in one row, indicating their identity. This portion of the tumor is more sclerotic than is usual.

the growing tumor assume independently a proliferation that transforms the individual liver lobule into a lobule of tumor tissue. This characteristic of the tumor seems also to have been observed by Dr. Travis in her case, but the process is so unique and of such significance in the question of the histogenesis of tumors that it seems to me to be worthy of considerable attention. The transformation of the liver lobule into tumor tissue seems to be the outcome of an increased activity of the proliferation at the margins of the lobule that was noted in the cirrhotic portions. Instead of being limited to the formation of a few little

columns of cells resembling bile ducts at the margin of the lobule the proliferation continues until all the lobule is replaced by such cells or until only a central island of liver cells remains. When this sort of proliferation has continued until most of the lobule has been transformed in the manner described, the columns of cells do not retain the appearance of simple new bile vessels, but instead they begin to grow in a disorderly manner until there is simply a mass of cells of embryonal type without grouping or form; the size of the individual cells also varies within a wide range. Occasionally there is a formation of a large amount of connective tissue between groups of the new cells, lead-

FIG. 4.

Section through tumor plug in portal vein. Here nearly all of the cells resemble liver cells, although of an embryonal type, and with little attempt at arrangement in columns. A cell with a giant nucleus is seen in the upper left-hand corner.

ing to formation of areas like those of a scirrhous carcinoma, but such appearances are unusual; generally the result is a mass of cells of varying shapes and sizes, with large and deep-stained nuclei, lying within the band of connective tissue that originally surrounded the lobule. Irregular karyokinesis, and uninuclear and multinuclear giant cells become abundant in the older of these areas; that is, in those nearer the centre. The rapidly growing cells seem to distend the lobular boundaries of fibrous tissue greatly, and often fuse through destruction of the connective tissue margins, but even in the oldest portions the lobular origin is usually distinct. There are but few capil-

laries in these masses of cells, and presumably for this reason in the centre of the large mass the central portions of the lobules are necrotic, while the cells near the connective tissue bands still remain alive.

So far as the above description has gone we are dealing with a type of carcinoma that might be referred to malignant proliferation of new-formed intralobular bile capillaries; but there are still other features which introduce a resemblance to tumors of true liver-cord cells. Among some of the islands of cancer cells there may often be found groups of cells whose cytoplasm, staining deeply and solidly with eosin, shows a strong resemblance to hepatic cells proper. This is generally seen in the lobules that have reached the largest size without necrosis. In the sections through the tumor thrombus in the portal vein this type of cell predominates, and there are here relatively few cells of the bile-duct type. Furthermore, in relation to the hepatic-cell part of the growth, it is not infrequently observed that in the lobules in which the periphery is being changed by proliferation of the bile-duct type, the liver cords in the centre also seem to change from the normal type, becoming larger, tortuous, and of the appearance seen in typical adenomas of liver cells.

It is to be specially noted that the changes seen in the liver lobules about the primary tumor do not occur in a regular centrifugal manner, but there are many lobules showing little or no proliferation that are much nearer the middle of the tumor than other lobules that have been entirely transformed into malignant tissue. The small secondary nodes around the primary one seem to be formed in this way by the starting up of malignant transformation in a lobule or group of lobules a little ways from the boundary of the primary growth. But there are no secondary nodules at any considerable distance from the primary tumor.

My interpretation of the development of this tumor is as follows: An alcoholic man was enabled to survive an atrophic cirrhosis with portal obstruction for an unusually long time because of the establishment of compensatory circulation through old peritoneal adhesions. As is usual in atrophic cirrhosis there was compensatory proliferation of the cells at the margins of the liver lobules, leading in some places to formation of adenoma-like nodules. At a point in the right lobe this proliferation continued beyond the normal bounds, and an area of malignant growth was formed, in just the same manner as carcinomas in other places are supposed to arise during the repair of wounds. But this carcinoma does not seem to have grown by direct extension in the usual way, with new tumor cells crowding out the pre-existing cells, but rather the existing cells themselves assume the power of proliferating in a malignant manner. Growth is, then, by an extension of the conditions that make malignant proliferation possible, whatever that may be.

This independent malignant transformation of cells in the vicinity of a tumor must be of some significance. That it should be observed particularly in the liver is, perhaps, due to the fact that the structure

of the organ makes its detection simpler than it would be in other places—a similar extension of proliferation has been described in the genesis of carcinoma of the skin,* growth occurring from the interpapillary projections of epithelium not in one single spot, but from many. Exactly what the significance may be is open to many interpretations.

In many of the reports of primary carcinoma of the liver one finds much discussion as to whether a certain growth arises from the bile ducts or from the hepatic cells. In the case under consideration both sorts can be found, with various degrees of transition between them. The explanation for this lies probably in the fact, which seems to have been generally overlooked, that bile-duct epithelium and the parenchyma cells are embryologically one. Therefore, in a malignant tumor in which reversion to the embryonal condition is a most important feature, it is quite natural that we should find the two types of cells both present. It was noticed in this case that where the cells were able to grow longest without suffering from pressure and loss of nutrition a larger proportion of the cells reached the liver-cell form—*e. g.*, in the lobules that had grown to considerable size without necrosis, and particularly in the tumor thrombus (Fig. 4).

A RÉSUMÉ OF SOME OF THE YEAR'S LITERATURE ON THE LIVER AND GALL-BLADDER.

By Herbert Swift Carter, M.D.,
of New York.

It is to be regretted that during the past year the purely medical aspect of this subject has not received the attention it merits and, compared to some other fields in medicine, there is little new to chronicle. However, more or less has been done to clear up the physiology of this gland and its adjunct, the gall-bladder; to develop aids in the diagnosis of its morbid conditions, point the way to rational forms of medical treatment, and to put some phases of the subject on a firmer surgical basis.

Anatomy and Histology. Naturally, with the careful study which has long been given this part of the subject, there is very little new recorded. Schaffer,[1] however, describes a specimen of liver injected with acid-carmine-gelatin from the portal vein in which the stain had passed into fine varicose canaliculi within the liver cells, and says that "the extreme importance of the passage of the injection from the vessels into such definite canals within the cells without ex-

* Peterson. Beitr. z. klin. Chir., vol. xxxii.

travásation and without injection of the bile canaliculi does not seem to have been appreciated, or, at any rate, it has not hitherto been published."

Bacteriology and Pathology. Among the most important contributions to medicine in the past two years has been that of putting the etiology of the formation of gallstones on a firm bacteriological basis. That the *sine qua non* of gallstones is bacterial there seems to be now no doubt, and the old theories of their causation have to be laid aside as insufficient. The fact remains, as has long been known, that certain predisposing causes to their formation are still as active as ever and obesity and a sedentary habit certainly have their place among these. Gallstones do not originate *de novo*, of that we are sure; and at the heart of every one of them there is probably a pathogenic bacterium.

The opinion as to the bactericidal action of bile is still somewhat divided. Thalma[2] says: "Bile contains a substance that checks the development of the colon bacillus, bacillus typhosus, and diphtheriæ. That the different bacteria vary greatly in their susceptibility to the action of bile (virulence as concerns the biliary passages being by no means synonymous with infectivity), that the bactericidal property of the bile varies at different times and in different animals, that the fate of the germs introduced into the bile ducts is largely dependent on their number, and that the hepatic cells and epithelium of the biliary passages exert a powerfully destructive action on bacteria, particularly on the bacillus diphtheriæ."

On the other hand, Lartigau,[3] who has carried on many interesting and instructive experiments on the bactericidal action of bile and the formation of gallstones, says: "1. Bile is not bactericidal to bacillus coli communis, bacillus typhosus, and some of the other pyogenic organisms (not specified). 2. Direct inoculations of the gall-bladder with different bacteria was followed by the formation of calculi. 3. Sterile, inert, foreign bodies in themselves do not give rise to this condition, although they and the stagnation of bile seem to favor the development of gallstones in the presence of infection of the gall-bladder."

Among the experiments from which he draws his conclusions is that of introducing sterile silk into the gall-bladder, and, again, of introducing infected silk. In the first instance no calculi are found, while in the latter they are produced very readily. The clinical proof bearing out this assertion is abundant, for one is often able to obtain a history of previous intestinal infection from typhoid or other causes, and, considering the frequency of intestinal inflammation, there are many ways in which the gall-bladder may obtain its necessary supply of micro-organisms, either by continuity or through the portal circulation; in fact, Fiedler says a normal gall-bladder is almost *never*

found. In his series of cases, however, he offers no explanation of the fact that women were found the victims of gallstones three times as frequently as men. Here, however, we have more usually the forenamed predisposing causes operating: obesity and sedentary habits.

TUMORS. But little reference is to be found to tumors of the liver and gall-bladder besides the usual report of cysts, secondary neoplastic deposits, etc.; but Modouiski[4] reports 4 cases of primary carcinoma of the common bile duct which with 37 others in literature make a total of 41; so the condition is unusually rare. In 16 the tumor was situated at the duodenal end of the common duct; in 7 of these it was confined to the papilla; in 11 the upper end of it was involved; and, again, in 7 the junction of the cystic and hepatic ducts was the seat of the tumor; in 6 the lower half of the duct; and in 8 no statement is made. So it will be seen that the two most common sites, by far, are the lower and upper ends of the common duct.

Dudgeon and Adaud[5] report a boy, aged fifteen years, with primary carcinoma of the liver of rapid growth accompanied by high fever. An unusual anomaly of extrauterine placental implantation on the liver is also among the curiosities of the year.[6]

DISEASES OF THE LIVER. Frank[7] gives a valuable résumé of primary tuberculosis of the liver, in which he quotes Osler and Hanot's classification of the condition, and concludes by saying that "A majority of the cases occur in children eleven to fifteen days old, in which the infection is in all probability usually through the umbilical vein from the placenta, and naturally, as such, presents little of practical interest to us as clinicians, as the diagnosis is for the most part only possible at the autopsy table."

Of unusual moment is the occurrence of abscess of the liver, due to the bacillus typhosus, years even after the original infection. An interesting case of this condition has lately occurred at the Presbyterian Hospital in the city of New York.

ACUTE YELLOW ATROPHY OF THE LIVER. The causes operating to produce this condition seem little by little to be narrowed down to the action of ptomains and toxins in the blood from definite groups of bacteria, and, although this cannot be proven in every case, still the frequency of a preceding condition predisposing to autointoxication, as we know it—*e. g.*, pregnancy—seems to stamp this disease as the resultant action of such agencies.

Harrison,[8] in reporting 3 cases of acute yellow atrophy, remarks that next to the degeneration in the liver the kidneys show the most marked changes; so he asks: "Is it not, then, logical to assume that the cause of the pregnancy kidney and acute yellow atrophy of the liver is to be sought in infection by bacterial poisons (ptomains and toxins) or in some sort of chemical agencies which form with special ease in

the pregnant condition? In a number of cases the bacterium coli communis appears to be an etiological factor."

In pseudocirrhosis of the liver we have an infrequent condition, and although the cause is as yet unknown, tuberculosis in the family history is of frequent occurrence and is observed in connection with similar conditions in other serous cavities. Strajesko[9] says the symptoms are the same as those of a real cirrhosis, not due to an interstitial growth of tissue, but to a thickening of the peritoneum over the liver, which produces the symptoms by contraction with pressure. The points to be kept in mind in recognizing the cases are: (*a*) A liver smaller than the normal. (*b*) A spleen which is not increased in size (contrary to the late manifestation in ordinary atrophic cirrhosis, probably because the peritoneum over it is also thickened). (*c*) An ascites which is quickly produced. (*d*) A frequently coexisting heart lesion.

Little has been added to our knowledge of ordinary cirrhosis of the liver, except the elaboration of the anastomotic circulation established after epiplopexy and its clearer understanding.

Syphilis. One of the most interesting and instructing papers of the year is that of Stockton[10] on syphilis of the liver; not in that it presents so much that is new, but reiterates facts so often lost sight of and left out of account in diagnosis. In this country too little has been made of this condition as a factor to be reckoned with, and Osler tersely remarks in discussing the subject to the effect not that the general practitioner sees visceral syphilis so seldom, but that he fails to recognize it so frequently. To quote Stockton more fully: "There is no fundamental difference between the pathology of congenital and acquired syphilis of the liver, for in either we may have: (*a*) Diffuse hepatitis or parenchymatous degeneration, to be succeeded by the ingrowth of fibroid tissue. These effects are probably due more to the local effect of the specific poison than to local infection. (*b*) Gummata occurring in large tumors, scattered masses, in miliary granulomata or in the budding stage, as mere aggregation of lymphoid cells. These changes seem to be the outcome of stimulation of the tissue from the *local* action of micro-organisms rather than intoxication. In some instances the liver is apparently invaded chiefly through the lymphatic system, when the liver is often attacked at its periphery; in still other cases the disease manifests itself especially in the blood-vessels. Among the clinical manifestations which may or will be mentioned here are: (*a*) Increased bulk of the liver. (*b*) Deformity of contour. (*c*) Roughening of adhesions to its surface. (*d*) Obstruction of the bile passages, causing jaundice. (*e*) Obstruction of the blood passages, causing ascites. (*f*) Perihepatitis (with friction, pain, and tenderness). (*g*) Rarely extraordinary enlargement of the liver, sometimes accompanied with pain, perihepatitis, and slight effusion,

which is apparently the result of lymphatic obstruction. In the early stages we find the liver congested, moderately enlarged, and functionally poor; these cases are usually classed as cirrhosis or carcinoma."

In this connection Flexner[11] gives some interesting statistics from the records of 5038 cases in the Philadelphia Hospital. He found hepatic syphilis 88 times in the following forms: 1. Interstitial, 44. 2. Gummatous, 23. 3. Perihepatic, 16. 4. Amyloid, 7.

Physiology. Since it is to physiology that we turn most naturally for our practical aids in medicine, the hope would be natural that each year would add materially to our store to help us in diagnosis and treatment; nothing startling, however, has been brought out during the past year, although much steady and painstaking experimentation has been done, which has laid another series of stones of the foundation for later investigators to build upon. The relation of bile to the lymph supply has been carefully studied by Bainbridge,[12] who follows along the lines laid down by Asher in 1899, when he injected ox-bile in blood serum and caused an increased flow of lymph from the thoracic duct, which he attributed to the increased metabolism of the liver, due to these substances. In Bainbridge's experiments he used:

1. Taurocholate of soda. Slow injection of small amounts invariably led to an increased flow of lymph, two or three times the normal amount, which began ten to twenty minutes after the injection and lasted about two hours. That this extra lymph is derived entirely from the liver is proved by there being no flow after ligation of the portal lymphatics on the injection of the sod. taurocholate.

2. Hæmoglobin in dilute solution did the same.

3. The tartrate, carbonate, chloride of ammonia also at times, but not so regularly.

All these substances increase the metabolism of the liver, and this being suddenly increased, he says, leads to the setting free in the liver cells of "crystalloid metabolites." These enter the surrounding lymph spaces, probably by diffusion, raise the osmotic pressure of the lymph, and abstract water from the blood, so accounting for the increased flow of lymph.

This experiment opens up an interesting field for discussion: first, as to its *modus operandi;* second, as to its possible usefulness in certain diseases. Its status is, of course, not yet fixed, but its usefulness may be at no distant time.

The relation of the liver to the metabolism of proteids, carbohydrates, and fats is an interesting subject for investigation, and Toepfer[13] has proven that the decomposition of albumin in the liver can take place only by aid of the intestinal canal. This is worked out by an ingenious experiment of "perfusion," by means of which the aorta is turned

directly into the portal vein; the stomach and intestines are then removed. He concludes:

1. When the liver was perfused with its own blood there was no accumulation of decomposition products in the blood.

2. This was also true when heterologous globulins and peptones were added to the blood.

3. After a simultaneous perfusion of the intestine and liver an increase in decomposition products was noted, which was also the case after extirpation of the kidneys.

It would therefore seem, he says, that the liver can decompose albumin in any considerable quantity only by aid of the intestinal canal. The relation of the liver to the metabolism of carbohydrates is, of course, more clearly understood, but that of its relation to glycosuria is still a field for discussion, particularly in the light of recent investigation by Herter and others.[14] Ewing, in discussing a paper of Herter's on this subject, epitomizes it by saying that if "Herter has succeeded in showing that an injection of adrenalin extract produces glycosuria; that the application of the substance to the pancreas produces glycosuria; that compression of the adrenal gland produces glycosuria, while compression of other glands does not; that tying off the vessels of the adrenals renders it impossible to produce glycosuria by ordinary means; that if, after extirpation of the pancreas, the glycosuria is diminished by tying off the adrenals, he has considerable evidence to show that the adrenal is very important in the pathology of human diabetes." These experiments of Herter's put the liver and adrenals in a very intimate relation, at least, so far as the production of glycosuria is concerned, and are among the most important contributions of the year to physiology.

The liver's relation to fat metabolism is as yet unknown, although Pavy claims that glycogen is transformed into fat in the liver; this, however, is denied by Claughey. All we know is that the liver cells take fat from the food and store it; as yet further investigation is needed to show its relation to actual fat metabolism, if any. That which is of special interest is the physiology of hepatic insufficiency and its relation to other diseases, especially Bright's; as the[15] "liver is probably the manufactory in which the greater part of the nitrogenous relics of broken-down products reach their final stage of urea," we would expect that in such a disease as chronic renal insufficiency (since it is through the kidneys that these products are largely excreted) we would have marked changes in the hepatic functions. Gouget[16] says: "In chronic Bright's, as a result of experiments in which urine or urea have been injected into animals, changes occur in the liver, due to the retention of urinary poisons which are stored up in the liver. It increases in volume and crystals of urea are found in the hepatic cells,

and cause changes from degeneration to cirrhosis, due to renal impermeability and are a result of physical rather than chemical action."

In the reverse condition, when we start with a diseased liver, Duchamp[17] has recently pointed out:

"1. In hepatic troubles in which a diminution of urea production takes place, the diuretic action of the urea is wanting and a notable falling off in the quantity of urine eliminated is the result.

"2. In advanced hepatic cirrhosis Bouchard has shown that a veritable anurea exists.

"3. The symptoms of renal alteration resulting from hepatic insufficiency include albuminuria, hyaline and granular casts, diminution of urinary toxicity, retardation of the elimination of methylene blue.

"4. Glycosuria, due to hepatic insufficiency, may show at first only after the evening meal, and is accompanied by a diminution in nitrogen elimination, urobilinuria, and indicanuria."

He also claims that administration of hepatic extract is rational treatment and its administration restores urea elimination and tends to abolish glycosuria.

A clinical discussion of these points would prove of interest, particularly as the sodium salts of the bile acids are now so highly recommended as stimulants to hepatic secretion and, in fact, as the only physiological stimulants of such. In this connection it is of interest to note the results of Croftan's[18] experiments with the bile pigments and bile acids, by which he claims to show:

1. Bile pigments and bile acids are not formed by the liver cells.

2. That they can be formed in various parts of the organism other than the liver.

3. That they can be formed from hæmoglobin outside the organism by a purely chemical, fermentative process, and without the intervention of the liver cells.

The influence of the liver on the coagulability of the blood is a most important, practical question; for, although Schäfer[19] showed that if the circulation of blood through the liver be stopped it loses its coagulability (in one-quarter of an hour in the dog) and is not restored for twenty-four hours, and that extreme jaundice has the same effect, no satisfactory explanation as yet has been given, and it, therefore, deserves our thought.

Diagnosis and Prognosis. Especially scanty is the year's literature on new, valuable aids in the diagnosis of liver and gall-bladder disease; not but that the journals have been full of articles on these subjects, but they contain mostly reports of cases, operations, and general statistics, and even these are largely confined to the gall-bladder.

Much confusion often exists at times in the differential diagnosis of

stomach, gall-bladder, and disease of the right kidney, stones, twists, abnormal mobility, etc. Boas[20] has sought to let the light in by means of electricity. He says that "in cholelithiasis one finds by electrization three tender points:

"1. Region of gall-bladder.

"2. At inferior border of liver.

"3. A more or less circumscribed area immediately to the right of the tenth to twelfth dorsal vertebræ. These points of tenderness are not pathognomonic, but are often useful in differential diagnosis, and as an indication of how treatment is progressing."

Jaundice in connection with stone in the common duct is, according to Mayo,[21] a very variable symptom: "In many cases so slight as not to attract special attention, and finding the stone was a surprise. In the majority, jaundice was marked. One case of extreme jaundice from impacted stone in cystic duct at its junction with the common duct and three cases of jaundice from malignant disease died from postoperative capillary oozing. In all these cases there were subcutaneous, ecchymotic spots, looking like purpura hæmorrhagica, before operation; every case of jaundice with this condition died in this way, and no case in which this was not present died from this cause (capillary oozing), although several were in extreme jeopardy."

In the diagnosis of hepatic insufficiency from any cause Strauss[22] shows that the degree of alimentary levulosurea is a good relative test of the integrity of the hepatic function. His method is to give 100 grammes of levulose on an empty stomach and test the urine passed in the subsequent four hours for the presence of levulose. He found in twenty-nine cases of liver disease twenty-six with an alimentary levulosurea. In fifty-eight persons with no known liver disease he found it six times, but these six might very well have had a moderate amount of hepatic insufficiency without knowing it.

Amœbic Abscess of Liver. Since the American occupation of the Philippines, cases of amœbic abscess of the liver are more common here, and if Van der Veer's statement[23] be only approximately correct, we may expect to find it in one-quarter of the cases of dysentery from this locality.

Osler[24] emphasizes the common error in diagnosis when a large liver abscess pushes up into the lung. A needle does not always clear the diagnosis. He illustrates it by five cases. He says, also, that in three of these there was practically *no leucocytosis*, and remarks that he must revise the statement in the next edition of his book dealing with this point, where he says leucocytosis is invariable.

In regard to rupture of the liver (and this applies probably equally to the other solid abdominal organs) Blake[25] insists on the importance of abdominal rigidity in *peritoneal irritation* as well as in actual inflam-

mation, for the blood in the abdominal cavity causes the rigidity even before the inflammation sets in.

The relation of pancreatic lithiasis to cholelithiasis from a diagnostic point of view has received little attention, although Kinnicutt[26] reports one case in detail of pancreatic stone, in which the diagnosis of gallstones had been made by von Leyden, and shows the extremely close similarity in the symptoms of the two diseases and the difficulties in diagnosis.

Gallstone ileus is a reflex condition to be kept in mind as a possibility after severe cases of colic.

TREATMENT. The recent literature on treatment resolves itself principally into the attempt either to dissolve gallstones *in situ*, to assist their expulsion or to prevent their formation, and are contributed largely by the ultra-conservative element in the profession, who make surgery the last possible resort. W. H. Thompson[27] maintains that only one case in thirty ever needs operative interference and recommends Carlsbad, sod. phosphate, or sod. sulphate every morning, changing off, to prevent the formation of stones; or olive oil, one to three ounces in hot milk, to help in their expulsion, as it is supposed to increase the flow of bile and mucus, and so aids in dissolving the gallstones. There are certainly cases in which this last seems to be followed by the passage of stones, but at best it is a most uncertain method and is usually disappointing, although it deserves a trial.

Since bile salts and particularly the sodium salts of glycocholic and taurocholic acid are both capable of dissolving stones outside the body, whether formed of pigment or cholesterin, it would seem more rational to give these salts to aid in the elimination of calculi or to prevent their formation. Richardson[28] recommends their trial. While we may be disappointed in their action as solvents, they are, as has already been stated, the most powerful physiological cholagogues in our possession, and have proved themselves extremely useful in clearing a sallow skin and an icteric tinge of the conjunctivæ, and are said to remove chloasma.[29] Keown recommends especially sodium glycocholate in the prevention of gallstones in cases of so-called torpid liver as found in alcoholism, drug habits, melancholia and its congeners, constipation and malaria; and, since bile increases the digestion of fats 50 per cent.,[30] it should prove a most useful adjunct in all wasting diseases. It is used by Richardson[28] in hepatic glycosuria with gangrene, substituting fats for starch in the food combined with thyroid extract to increase oxidation, of each two and one-half grains.

Clemm[31] uses eunatrol, which is an acid oleate of sodium, for the prevention of gallstones, and believes all cases of uncomplicated cholelithiasis are curable by its use. He thinks it is stored in the liver and exercises its function in dissolving stones.

In the treatment of hepatic syphilis, Cabot[32] calls attention to the fact that it is in some cases impossible for a time to affect visceral syphilis by antisyphilitic treatment, and it is only by building up the general health that, in conjunction with the specific remedies, anything can be accomplished. He also says that the therapeutic test of Justus for diagnosing syphilis is very unreliable, and Flexner adds[11] that the outlook for syphilitic interstitial hepatitis is less favorable than in the gummatous form, although if the condition is not advanced it is more favorable than non-syphilitic cirrhosis.

In relieving itching associated with jaundice and in clearing the skin and conjunctivæ of icterus, if the statement of Sinhr[33] is correct, we may hope for better success by using the fresh bark of the root of Moringa pterygosperma (horseradish), one drachm, three times a day, of the paste freshly prepared. In several cases in which he used this the skin was cleared in four to five days. This seems at least rational when we remember how these patients crave condiments, and the appetite is often a good indication of what the organism needs.

Surgical Treatment. Although supposed to deal principally with the medical aspect of the subject, still one must take into account and know the present status of it from a surgical point of view; what cases are suitable for operation; when to operate; and what the best recognized procedures are. The past year has seen an immense amount of surgery, especially of the gall-bladder, and to a less degree of the liver.

The surgical enthusiasm, however, will probably be toned down to a rational basis, and surgeons will recognize that many cases of gallstones can live comfortably for years, to a ripe old age even, after one or more attacks of colic, without their attentions, as evidenced by the frequency with which gallstones are found post-mortem and often even without the history of a single symptom referable to that part of the anatomy. The most radical opinion of the subject is perhaps best expressed by Park,[34] who draws a comparison between the appendix and gall-bladder as follows:

1. Both are hollow receptacles, tubular, and contain a certain amount of secretion.
2. Both are lined with mucous membrane, and the secretion, when readily discharged, causes no trouble.
3. Calculi may be deposited in each from their secretions.
4. They are both, at times, anchored to surrounding tissues.
5. They both cause localized pain.
6. Each have a fulminating and a growing process.
7. As the appendix disturbs the function of the colon, so the gall-bladder does of the stomach and pancreas.
8. He believes in treating them alike and recommends ablation of gall-bladder, if at all diseased.

A more moderate tone is assumed by Strobell[35] in making the simple presence of gallstones an elective indication for operation, while the imperative indications are:

1. Acute inflammatory conditions from bacterial infection cholecystitis, infective, ulcerative, suppurative, or gangrenous.

2. Impaction of stone in the cystic and common duct.

Still less radical is the opinion of another surgeon, Berg,[36] who presents the fairest classification from an operative point of view.

(*a*) *Medical Treatment.* Is indicated in cholecystitic pain and attacks of biliary colic, in *either case* unattended by fever.

(*b*) *Surgical Treatment.* 1. Operations of choice in (*a*) severe cholecystitic pain or oft-repeated, uncomplicated attacks of biliary colic, persisting in spite of medical treatment; (*b*) after the first attack of acute cholecystitis associated with fever.

2. Compulsory operations. (*a*) Intensely acute attacks of cholecystitis, which may be the first indication of calculous disease. (*b*) Hydrops, empyema, gangrene, perforation of the gall-blader, cholæmia (?), abscess of the liver and diffuse peritonitis.

As to the kind of operation, when surgical interference is necessary, that, naturally, must be left to the surgeon, and whether a simple cholecystotomy or an ablation is best must be a matter for surgical opinion alone. However, in view of the tendency to the latter operation, no less an authority than Bland Sutton[37] says he has found it necessary to remove the gall-bladder but six times. Of course, the English surgeon is extremely conservative.

Hepatic Abscess. In the treatment of hepatic abscess, contrary to our generally accepted surgical ideas, Manson[38] contends for the use of the needle or trocar and canula, and says:

1. Pus should be sought early, as soon as there is even a suspicion of abscess.

2. It is safe with certain precautions (not stated) to use these methods.

3. It is unnecessary to expose the surface of liver before operation.

4. He regards the operation of transpleural hepatotomy as heroic.

Maitland[39] expresses the sounder opinion when he objects to the exploring needle on account of the danger of hemorrhage and peritonitis, or, if the puncture shows pus, operation must immediately follow.

Probably the most interesting feature of the surgical side of the subject to medical men is the present status of operative interference in cirrhosis, and, unless one understands clearly the indications, no less than the object to be gained, one may easily be led into a too enthusiastic support of this newer method of cure.

In 1893 Hale[40] collected a series of twenty-four cases of cirrhosis with ascites, in which he showed that from the first tapping (in fourteen

to the deaths of the patients the average time was sixty-three days; while in ten who were not tapped, death came in an average of sixty days from the beginning of the abdominal enlargement; showing that paracentesis is of doubtful usefulness, except in relieving the patient's distress.

These figures have also been corroborated by Converse[41] in the past year. Hale also said that "If a patient survives a long time, the ascites is probably due to complications, such as chronic peritonitis and perihepatitis. Therefore, these complications make for a longer life."

It probably follows, however, in the light of operative successes that these complications did not cause the ascites, but that the cases lived longer because the effects of the cirrhosis on the portal system were obviated by the development of these same complications with the establishment of a collateral circulation, which we know now is the object to be sought by operation. It is nevertheless true that, although Hale's conclusions were at fault, he unconsciously pointed the way to operative interference by his observations.

Packard and Le Conte[42] report twenty-two cases of cirrhosis treated by operation, and Montgomery sixteen, making in all thirty-eight, with results tabulated as follows:

Recovered	15	=	39.4 per cent.
Improved	4	=	10.5 "
Unimproved	9	=	23.6 "
Deaths	10	=	26.3 "

This represents rather an unfairly high mortality, as the cases were not selected, and there are included those who should never have been operated upon at all.

The fairest conclusions on the subject of operation and its contra-indication seem to be those expressed by Lord and Sears[43] in saying that the "conclusion seems reasonable that operative measures are never justified in the presence of jaundice, and rarely with a history of hemorrhage from the digestive tract, since the fibrotic changes in the liver are probably so far advanced as to cut off expectation of greatly prolonging life. But, when practically sound heart and kidneys exist, and the general nutrition is so well maintained as to show that sufficient glandular structure still remains in the liver to maintain its function, and when competent medical treatment has failed, operation may be considered."

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THE RELATION OF CERTAIN ADENOCARCINOMATA TO ATROPHIC SCIRRHUS OF THE BREAST.

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Under this topic the following questions arise:

1. Is there a distinctive tumor of the breast properly described by the name atrophic or atrophying scirrhus?

2. Is operative procedure for relief of such tumors to be advised against, because experience has shown that such an operation quite uniformly fails to prevent recurrence and thus shortens life, as recurrences are much more malignant than the original growth?

3. Can these tumors be morphologically distinguished from other malignant tumors of the breast, and do their microscopic characteristics explain their slighter malignancy?

It seems probable that all three of these queries can be answered in the affirmative, although this may be disputed by some authorities except as to the first.

I think that most surgeons will admit that they have observed certain cancers of the breast, occurring mainly in patients over sixty years of age, which merit the title of atrophying scirrhus by their clinical course. They resemble other forms of breast cancer in their early manifestations, but proceed slowly until the skin is involved, after which they seem to cease to grow and the ulcer shrinks and becomes hard and highly colored, giving origin to the lay name of "rose cancer." In this condition, either as an ulcer with slight discharge or as a dry, scaling depression, this form of cancer may persist for many years with little annoyance to the patient and practically no interference with her general health.

Most of the older authors recognize this form of growth, and mention its comparative benignancy and the long periods which may elapse without other than local symptoms. The later authors, however, are inclined to ignore it, perhaps because modern surgical methods have tended to the removal of all breast tumors before reaching the stage at which the atrophic tendency would manifest itself.

Butlin, in the *International Cyclopædia of Surgery*, 1884, figures the atrophic scirrhus and advises against its removal, "for it sometimes appears as if a disease which was previously quiescent and likely to remain almost unchanged during years is started into fresh activity and power which would never have been looked for in the primary disease."

Gross says: "In atrophying scirrhus the epithelial elements undergo fatty degeneration whereby they are partly converted into a granular emulsion which is absorbed, while the contracting stroma renders the alveoli smaller and narrower until in advanced stages they are merely fusiform clefts which contain fatty detritus or one or more rows of unchanged cells."

This same description is copied by Parks, Wharton and Curtis, *American Text-book* and *International Text-book of Surgery*, but none of these lay any stress on the chronic clinical course as a contraindication to operation. Dennis, in his *System*, gives a good description, but fails to give any indication as to operation. Tillman entirely fails to mention it.

Shields' *Diseases of the Breast*, 1898, is the only recent book which gives this subject any attention, and his description is by far the best. His statement is as follows:

"Atrophic degeneration of scirrhus is very important from a clinical point of view. It appears to be caused by diminution of vascular supply, and hence is commonly found in spare and thin persons, in the

aged and weak, and in those whose circulation is feeble. This is not universally the case, however, and the cause of this important degeneration is not quite clear. Microscopically, the growth closely simulates fibrous tissue, and with some difficulty collections of atrophic cells and débris are here and there found by the observer, which mark the true nature of the affection. It would be difficult enough, however, for any pathologist apart from clinical assistance to distinguish a section of old atrophic cancer from scar-tissue."

Again, pages 333 and 334:

"All writers notice instances of atrophic or withering cancer. It is usually seen in old and spare persons, and its puckered, cicatricial condition is beautifully shown in the plate. Sometimes slight ulceration is observed, and part of it is often covered by a scab. The glands are very seldom affected. These patients often do not seek advice until the disease has existed for many years, and consequently the surgeon must be especially cautious that internal metastases do not already exist. These are the cases of cancer upon which charlatans found their reputations, and in which I am bound to state members of the profession so often give erroneous opinions.

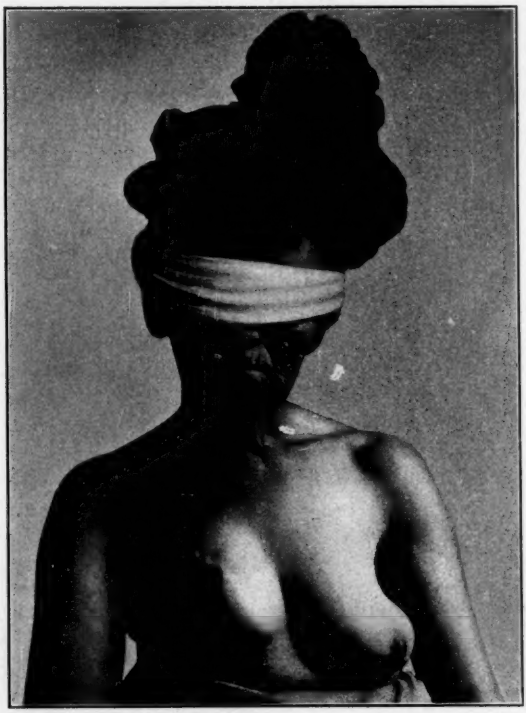
"Bryant in his work relates an excellent and striking series of atrophic cancers, where the patients survived seventeen, fifteen, twenty, nine, and eight years. In one secondary deposits of the skin disappeared and 'fell off' from the fibrous contraction of the tumor. Such experience is not singular. Gross devotes a considerable portion of his book on tumors of the mamma to this interesting class of cancer. He points out that though patients may live with atrophic scirrhus for a quarter of a century, yet visceral deposits are very frequent, and it ultimately invariably destroys life. The skin and fascia of the chest usually ultimately become extensively implicated, and so in the end are the axillary glands. He gives the average age of the affection at forty-seven years. The average period of life in eight cases was no less than fourteen years and nine months. Personally, the cases I have observed of this affection have been principally in old women of seventy years of age and upwards, and notwithstanding the experience of Gross I am inclined to look upon it generally as the cancer of old age, though notable exceptions may be quoted to this rule. In my own experience the axillary glands have not been affected, though the disease had been present in the breast for years, and this is a very remarkable point in a very curious malady."

The photograph gives a typical atrophic scirrhus.

The quotation from Butlin expresses quite accurately the opinion of the older writers as to the propriety of operations upon atrophic scirrhus, but the recent text-books and writers on surgery seem to be almost unanimous in ignoring any special indication in these cases.

One of the best known workers in this branch of surgical pathology, who is in touch with the work done at a large clinic where special attention is paid to breast surgery, said that he recognized no such tumor nor any indication against operation upon any form of breast carcinoma.

FIG. 1.



Atrophic scirrhus of six years' duration. The patient was an old-maid, aged sixty years. The nodule above the dry depression was due to a needle puncture through the edge of the tumor in the early stage of an injection treatment, which was then discontinued. The patient died one year later of acute disease without progress in the tumor.

In contrast to this is Shields' advice in the work quoted, page 386: "Though it is now customary to remove well-marked atrophic carcinoma, I doubt that, especially in elderly women, this course is at all advisable. The records of these remarkable cases make it clear that they may live so long in comfort without surgical interference, that my personal feeling is strongly in favor of adhering to the ancient

principles of surgery and leaving them entirely alone, especially if the patient be over sixty years of age. We have yet no evidence that the removal of atrophic carcinoma will prevent subsequent visceral or osseous deposits."

The singularly favorable results attained by Halsted and others in breast surgery have created an optimistic spirit in many quarters which has overruled the teachings of experience in these cases of atrophic scirrhus.

Many surgeons have certainly had the misfortune to observe prompt transformation of a sluggish, quiescent disease by operation and prompt recurrence into the most malignant form of cancer. It seems probable that the results of operation as to recurrence in this class of cases are distinctly worse than in cases of ordinary carcinoma of the breast, and also that the recurring tumor, in this as well as other types of cancer, is vastly more malignant than the primary growth. Microscopically, it is the rule that recurrences are of more malignant type than the primary growths, a characteristic feature being a scanty, ill-formed stroma, forming very small alveoli with few cells in each alveolus.

In answering the third question, it must be noted that all authors seem to have copied an old description which assumes a fatty degeneration of the cells, with contraction of the stroma as the essence of the atrophic scirrhus. These changes undoubtedly do take place in many cases of scirrhus of the breast, in some part of the tumor, but such changes are not incompatible with great malignancy.

I have been unable to secure any sections of atrophic scirrhus which substantiated the statement that the above description applied to this growth, but I here submit drawings of sections from three tumors which belong to this class, which all show adenomatous features, which demonstrate that in these few cases at least the relative clinical benignancy was inherent and dependent on morphological peculiarities and not upon degenerative changes.

These sections will further demonstrate why these growths might easily be diagnosed scirrhus, and would invariably be so if the old dictum of cutting sections for diagnosis from the advancing edge of the tumor were followed.

The study of a large number of sections of various varieties of breast carcinoma has given me the impression that in nearly every case the advancing edge presents the scirrhus picture in some fields, and this may be true even of infiltrating sarcomata; and that in order to make a correct diagnosis the older and central portions of the tumor must be studied.

The drawings[1] submitted are from sections of three atrophic cancers,

[1] I am indebted to Margaret S. Nickerson, of the University of Minnesota, for the camera-lucida drawings below.

two of the breast proper and one of the submammary fold, which are all true adenocarcinomata, all exceedingly chronic in their clinical course, all presenting an advancing edge which simulated true scirrhus.

CASE I. *Cancer of Submammary Fold.*—Mrs. A., aged forty-two years, French-Canadian, married, a patient of Dr. J. E. Moore, to whom I am indebted for the clinical history, was seen first in July, 1898, when she had a small, indurated ulcer in the submammary fold of right breast, which had been present for a long time—some years. Physical examination showed dulness of right chest and anterior mediastinum, and this was supposed to be due to malignant deposit, and operation was consequently refused.

She improved after this; the pulmonary dulness disappeared, and the ulcer made little headway.

FIG. 2.

Photograph of Case I., showing removed breast with ulcer of submammary fold.

In 1900, two years after the first examination, the ulcer was little, if any, larger than at first, but her general condition was better, and she being very anxious for operation, the tumor and breast were removed. She died of pulmonary complications within six months. As there was no post-mortem the existence of metastases can be only surmised.

The breast shows no cancer; in the skin of the submammary fold is a tumor dipping down about one-half inch in depth and extending in the skin about one inch each way from the angle. There is also an infiltration of the pectoral muscles and connective tissue, extending not over one inch from the primary growth.

Sections from the angle of the ulcer show an adenocarcinoma having a good deal of stroma, forming irregular alveoli containing irregularly cuboidal cells. In all sections from the older part of the tumor there are

alveoli containig a single row of cells, with distinct lumen; but as sections are cut further away from the centre the cells become more atypical in shape and arrangement, and finally in the muscle and connective tissue infiltrations all trace of adenoma is lost and a pure scirrhus picture is seen.

FIG. 3.

CASE I. A schematic low-power sketch, showing a general view of the cross-section of the new-growth. Only the bottom of the sulcus is seen to be ulcerated. The letters show the fields from which the other drawings were made with camera lucida. × 10.

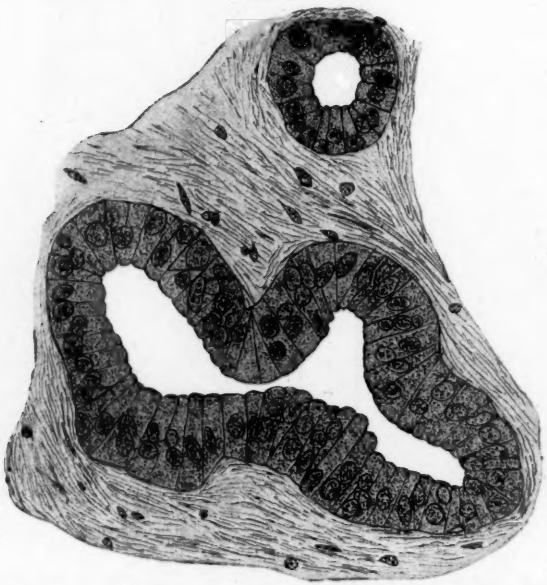
Shields describes a tumor clinically like this, except more acute, in a woman aged seventy-three years, which he says was scirrhus arising in peripheral lobule of the breast.

I am indebted to Dr. F. F. Wesbrook for the following history, the tumor coming to him for diagnosis from the practice of an irregular who was using an injection treatment.

CASE II.—The patient was an old-maid school-teacher, aged forty-two years, who had always been healthy. She had known of the tumor in her breast for over five years. After a prolonged injection treatment the tumor was removed with breast and axillary glands. There was recurrence within six months, local and general, and death a few months later.

The tumor consisted of a small nodule near the nipple, not encapsulated, and not infiltrating the muscle. Microscopically the tumor cannot be distinguished from the one from which the drawings were made. Like this, the superficial, older parts of tumor were adenocarcinoma, while the younger, advancing edge was in appearance scirrhus.

FIG. 4.



Gives a high-power detail drawing of a single acinus from field A. × 440.

This case, while in a comparatively young subject, showed the chronicity of history and prompt recurrence after irritation and operation which is so characteristic of the atrophic scirrhus.

CASE III.—An old-maid, aged fifty-eight years; general health good. The tumor had been present fourteen years and had ulcerated for several years, with frequent large hemorrhages. There was marked enlargement of the axillary lymph nodes. The breast was removed without opening the axilla and the patient made a good recovery, and was well and without recurrence two years later. The axillary lymph nodes became smaller soon after the operation.

An examination of the gross specimen shows a rather large breast with an ulcerated surface about three inches across in its upper and

FIG. 5. FIG. 6.

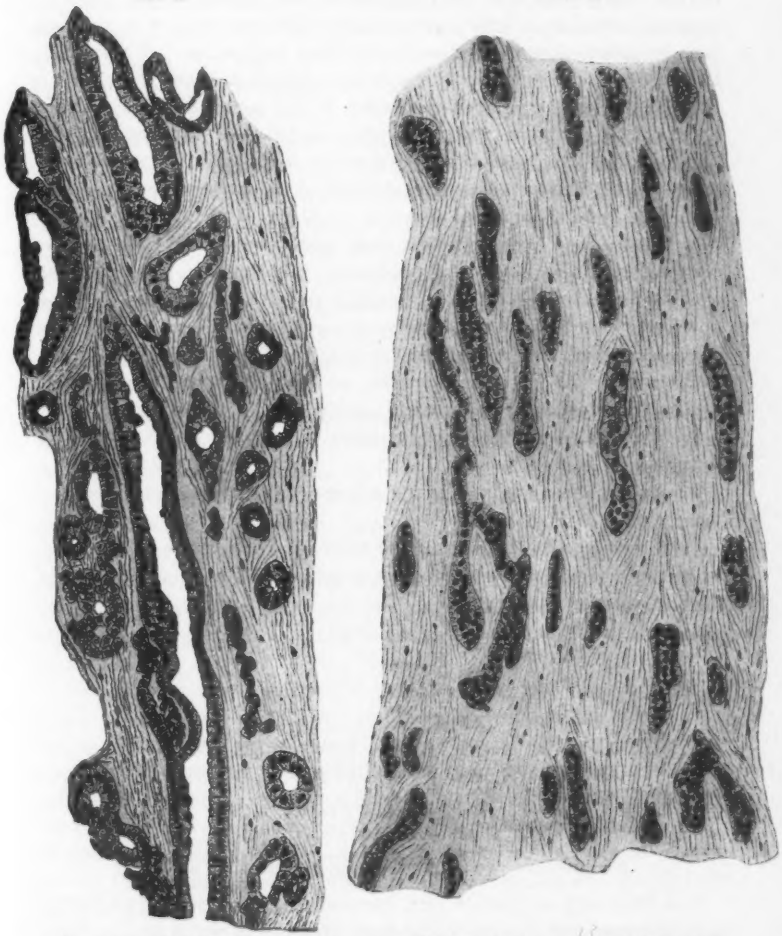


FIG. 5 shows field B of Fig. 3, and gives a general idea of the arrangement of the adenomatous tissue. × 140.

FIG. 6 shows a drawing from field C, and illustrates clearly the scirrhus picture presented by the advancing edge of the new growth. × 140.

outer quadrant. The tumor is confined to an area about one-half an inch deep below the ulcer, but shows no encapsulation. The microscope shows a cylindrical-celled adenocarcinoma in areas near the sur-

face of the ulcer, and more cuboidal-celled, scirrhus-like infiltration of its advancing edge.

The old classical view of this tumor being an ordinary scirrhus with fibrous overgrowth and fatty degeneration of the cells has probably a certain number of histological examinations to support it, as it has been accepted without question by so many authorities, but personally I have never happened to see a section substantiating this view.

On the other hand, adenocarcinoma of the breast is not mentioned by the writers above noted, with the exception of Halsted, and the *International Text-book*, which quotes his work, and the adenocarcinoma which Halsted figures is entirely different, histologically and clinically, from those noted above.

Is it not fair to presume that if these three tumors could come under observation at one laboratory, especially far from the great centres where such material is abundant, that more of these atrophic cancers, if all were studied by the microscope, might be found to have an adenomatous element which would justify their greater benignancy?

SUMMARY. 1. The term atrophic scirrhus is worthy of retention as describing an important clinical entity.

2. It is extremely doubtful whether such cases are benefited by operation.

3. Certain adenocarcinoma of the breast have the clinical history of the atrophic scirrhus.

4. It seems probable that if more of these tumors were studied histologically they might prove to have an adenomatous element to justify their comparative benignancy.

REPORT OF TWO CASES OF ULCERATIVE ANGINA AND STOMATITIS, ASSOCIATED WITH THE FUSIFORM BACILLUS AND SPIRILLUM OF VINCENT.

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THE February number of THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES for the preceding year contains a report by Dr. Emil Mayer of one case of membranous angina and stomatitis associated with the fusiform bacillus and spirillum of Vincent, with a brief review of several articles published abroad. In view of the number of cases reported in Germany and France, he comments upon the absence of any English literature upon the subject, leading us to infer that the affection must be rare in this country.

It seems probable, however, that the deficiency may be partially explained by the neglect in recording cases, by lack of bacteriological examinations of fresh specimens, and difficulty in making a differential diagnosis clinically between this affection and syphilitic disease of the throat and mouth, or by the possibility that the angina or stomatitis, giving rise, as they do, to such mild symptoms, may be disregarded by the sufferer or treated by home remedies.

Vincent[1] first pointed out, in 1896, that certain types of ulcerative angina were associated with a fusiform bacillus and a spirillum, and two years later he reported[2] fourteen cases and spoke of the condition as a diphtheroid angina. In 1887 Bernheim[3] published his researches in thirty similar cases of angina and stomatitis, but he hesitated to consider the fusiform bacillus and spirillum as *the* etiological factor. Niclot and Marotte[4] gave an exhaustive description of the bacteriology of this condition, of which the following is an epitome:

The bacteriological characteristics of this affection of the mouth and throat is the almost constant *combination* of the fusiform bacillus and spirillum of Vincent.

The fusiform bacillus is swollen at the centre, with pointed extremities. It is generally straight, but is sometimes curved or bent upon itself and measures 6μ to 12μ. It is encountered in irregular masses, often as a diplobacillus, and sometimes two are seen lying at an angle to each other. The motility has been questioned by a few, but is maintained by Niclot and Marotte. The bacilli stain readily with the basic stains, but are generally decolorized by Gram's method. The involution forms sometimes resist the decolorizing agent, and occasionally show a vacuolation or granulation, but never a demonstrable spore formation.

The dimensions of the spirilla vary, but they are very long and of equal width throughout. They are observed singly, in groups, and are sometimes seen in an inextricable mass. Their motility may be retained for many hours, but diminishes rapidly on exposure to air or cold. The staining reaction differs from that of the bacilli only by the fact that the spirilla are invariably decolorized by Gram's method. Where the disease process is superficial the spirillum may be absent, but in the deeper lesions the combination of bacillus and spirillum is invariable.

In the superficial parts of the ulceration one finds Vincent's bacillus and spirillum associated with the streptococcus, pneumococcus, colon, and Klebs-Loeffler bacillus, but in the deeper parts only the bacillus and spirillum in their characteristic combination are found. Cultivation and inoculation have so far given negative results, unless com-

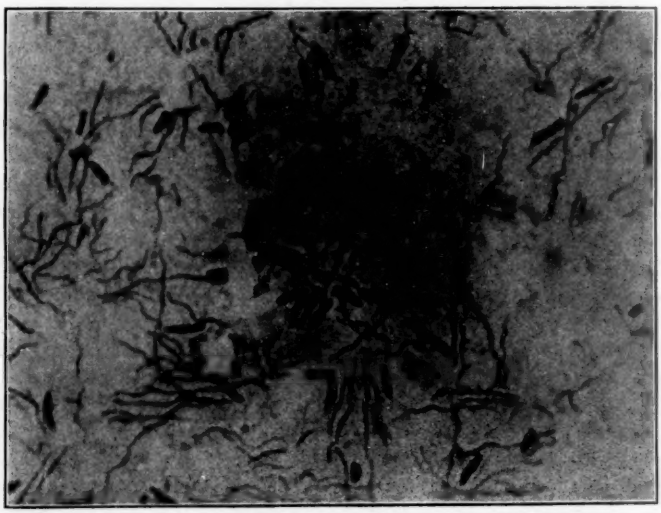
[1] Annales de l'Institut Pasteur, 1896.
[2] Bull. de la Soc. des Hôpitaux, March, 1898.
[3] Deutsche med. Wochenschr., 1897.
[4] Revue de Médecine, April 10, 1901.

bined with the streptococcus, when, after the "third passage," Niclot and Marotte recovered them from the mucus of the dysenteric discharges of a dog.

My own observations have been limited to two cases, one of which seemed of special interest on account of the ulceration of the alveolar process following the extraction of a tooth.

The first case occurred in the service of Dr. A. C. Thomas, to whose courtesy I am indebted for the opportunity to observe the disease:

CASE I.—The patient, a rather frail young man, twenty years of age, employed at the Connecticut Hospital for the Insane, consulted the physician for a sore throat of several days' standing.



The bacilli and spirilla of Vincent as seen in the first case. Stained with dilute carbol-fuchsin and magnified 1500.

His family history was excellent; father, mother, and several brothers and sisters were all living and well; no other member of the family had ever suffered from sore throat, except one sister, who had a mild attack of diphtheria a few years ago. The young man had had the usual diseases of childhood without residuals, and had always been well, although not robust. His habits were exemplary, and venereal disease was positively denied. One year prior to this attack he suffered from diphtheria, the constitutional symptoms of which, he claimed, were mild, but he was isolated for several weeks on account of the persistence of the Klebs-Loeffler bacilli in the throat.

The sore throat for which he sought treatment caused him little discomfort except upon deglutition, but there was a constant feeling of soreness and itching, which did not inconvenience him sufficiently to

interfere with his regular work. There was no glandular enlargement and very little increase in amount of saliva.

Four weeks previous to this time he had taken gas (to which he attributed his trouble) for the extraction of the last molar tooth on the left side of the lower jaw. One week later the gums became hyperæmic, and he discovered that the site of the tooth was covered with an irregular superficial ulcer, the floor of which was composed of a rusty-gray membranous exudate. From that time until he came under observation, three weeks later, the gums were never free from one or more of these patches. He experienced no particular inconvenience from these, until the tonsils became involved, between two and three weeks after the appearance of the first ulcer. At this time his temperature was 99°, pulse was full and regular, and he felt well, with the exception of the slight soreness in the throat.

Examination of the throat revealed rather large ulcers involving the greater portion of each tonsil and encroaching slightly upon the uvula. These ulcers were rather superficial, with irregular, inflamed edges, the floor being covered with a grayish membranous exudate, which was removed without difficulty, but re-formed rapidly. The slightest touch upon one of these areas left a bleeding surface. Small patches resembling those on the tonsils were present at the site of the extracted tooth, on the corresponding area of the lower jaw, and on the gum above the left upper bicuspid tooth.

Spreads and cultures from all these localities showed the same characteristics at three successive examinations, viz., red blood corpuscles, degenerated polymorphonuclear neutrophiles, and broken-down epithelial cells. The bacteria present were a few diplococci and very numerous bacilli and spirilla.

Morphologically, the bacilli were from 5μ to 10μ in length and quite thick. Some were larger at one extremity than at the other; many were swollen in the centre, with pointed extremities, while a few were curved like a comma. The majority were straight and often occurred as diplobacilli, while they were frequently seen in groups or lying at an angle of 60 to 80 degrees to each other. They were actively motile at first, but lost their motility in a few hours. The majority of them were decolorized by Gram's method, but stained well with the basic stains. A few of them when stained with Loeffler's alkaline methylene blue gave the impression of vacuoles, but no spores could be demonstrated, and in other stains this apparent vacuolation was absent. Efforts in staining for flagella were unsuccessful. The spirilla were 25μ to 40μ in length, but very slender. They were completely decolorized by Gram's method; otherwise they reacted to stains precisely as did the bacilli. They, like the bacilli, were actively motile at first, but lost their activity entirely after a few hours in bouillon.

The cultures made on blood serum showed a lance-shaped diplococcus and a very short bacillus, which was occasionally swollen in the middle, with pointed extremities, but was usually attenuated in the centre with bulbous ends. This, however, could not possibly be identified with the original bacillus as seen in the spreads. The other cultures on bouillon, agar, glycerin-agar, gelatin, litmus gelatin, litmus milk, etc., showed only pneumococci and large spore-bearing bacilli in threads. The cultures were all grown aërobically, and were under observation for sixty-two hours.

The patches on the tonsils and gums gradually disappeared under mild antiseptic treatment, and the mouth was entirely well three weeks after the involvement of the tonsils and six weeks from the appearance of the initial lesion.

CASE II.—The patient was a well-developed and nourished German woman, aged thirty-six years, who was admitted to the Connecticut Hospital for the Insane, November 24, 1902, suffering from manic-depressive insanity, maniacal form, of one week's duration.

She was the mother of eight children, the youngest being some ten weeks old. Childbirth and lactation were the assigned causes of insanity, but she seemed in good physical condition, and an examination of the blood gave a slight increase of both erythrocytes and leucocytes as follows: hæmoglobin, 92 per cent.; erythrocytes, 5,536,666; leucocytes, 9,200; polymorphonuclear neutrophiles, 75 per cent.; small lymphocytes, 16.2 per cent.; large lymphocytes, 7 per cent.; eosinophiles, 1.4 per cent.; mast-cells, 0.2 per cent.; myelocytes, 0.2 per cent.

Her family and personal history were negative. During her periods of marked psychomotor unrest she talked incessantly and refused food. She was constantly moistening her dry, cracked lips with her tongue, in doing which her tongue came in contact with her partially closed teeth. This irritation caused a hyperæmia, which finally resulted in an abrasion of the mucous membrane along the edges of the tongue. This surface soon became a superficial ulcer, covered with a creamy exudate, which assumed a membranous character and was very adherent. A few days later a similar exudate appeared along the border of the lower gums, which was, however, easily removed, leaving a bleeding surface. Salivation was not marked, nor were the glands enlarged, but the fetor was excessive. The temperature was normal, and the patient made no complaint except to utilize her sore mouth as an excuse for not eating.

Several bacteriological examinations of scrapings from the diseased areas showed the bacillus and spirillum of Vincent, accompanied by a large number of staphylococci and a few large non-motile bacilli stained by Gram's method. The bacilli (Vincent) were less motile than in the first case, but the spirilla were quite as active. The majority of the cultures produced a pure growth of staphylococcus albus, while others were associated with a large spore-bearing bacillus. Under daily applications of silver nitrate the stomatitis disappeared in about three weeks.

The clinical diagnosis in the last case was gangrenous stomatitis. A stomatitis of this character has occasionally been recorded among insane patients, and it would be very interesting to know how many of these cases would have revealed the presence of the bacillus and spirillum of Vincent if bacteriological examinations had been made. Unfortunately, there is no record of any investigations along this line. Both of these cases apparently had their origin in a slight trauma, the first in the extraction of a tooth, the second in the abrasion of the mucous membrane of the tongue from rubbing against the teeth.

The duration of the affection, as described by Vincent, Bernheim, and others, varies from ten days to six weeks, and there is a tendency toward a spontaneous cure. Consequently, little is known of the

pathological anatomy of the condition, as no deaths are recorded from this disease, when uncomplicated. I find no evidence that the disease is communicated easily from one individual to another, and the absence of constitutional symptoms excludes the production, or rather the absorption, of toxins.

The study of cases of this character is specially valuable, not only for the importance of the disease itself, but as an aid in differentiating it from diphtheria and syphilitic affections, which it so closely resembles clinically.

Viewed in this light it assumes an importance it otherwise could not claim, and it is surely worth while to give the patient the benefit of a thorough bacteriological examination of both spreads and cultures in every case of suspected diphtheria or syphilis before subjecting them to a possibly unnecessary course of medication.

THE "IDIOPATHIC" OR "ESSENTIAL" DROPSIES OF CHILDHOOD.

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During the summer of 1902 a number of cases of unexplained œdema came under the observation of the writer in the wards of the Boston Floating Hospital for Children. On reference to the text-books on diseases of children for an explanation of the phenomenon, it was found that, with one or two exceptions, the subject had received either very brief mention or no consideration at all.

Receiving at that time but little assistance from the text-books, the writer sought to find in the general literature some description of similar cases. In view of his experience with the text-books he was not prepared to find a literature very voluminous or interesting. Quite the contrary has, however, been the fact. As report after report of these or allied cases was found the subject became one of ever-increasing interest.

This fact must be the writer's apology for the desire to report cases from his own limited experience.

The characteristic feature of this condition is the appearance of œdema, in one or more parts of the body, *without albuminuria* or *sedimentary evidence of organic disease of the kidneys; without clinical* or *post-mortem* evidence of *organic disease* of the *heart* or *kidneys*.

It may occur in children of any age, but is not by any means limited to the age of childhood.

It occurs in children who previous to and *during its presence* are *otherwise well;* or it occurs, accompanied by symptoms more or less peculiar to it, in children previously and subsequently well, or, finally, it occurs immediately preceding, accompanying, or immediately succeeding some disease other than the organic conditions above mentioned.

The coincident symptoms of the second class are only collectively, not individually, peculiar to the affection.

The condition may be acute, subacute, or chronic in its onset or in its course.

We see by the above classification that it may be apparently primary or apparently secondary. The term apparently is here employed since, as will be shown later, we cannot say in any given case that it is *positively* primary or *definitely secondary.*

Mention will be made further on of the conditions in which this affection has been regarded as secondary; also of different types of the disease, both primary and secondary. It may now be of interest to make brief mention of several cases coming under the writer's personal notice.

The following nine cases seem all to come under the category of "apparently" secondary cases, in that they all occurred in the course of or following some other pathological condition:

Case I.—J. T., boy, aged thirteen months. Father died from "brain trouble." Family history otherwise negative. Past history elicited from the mother showed no knowledge of any rash or infectious disease. He was nursed for four months, when oatmeal-water was added as supplementary nourishment up to the tenth month, since which "Mellin's Food" has been given.

Three months ago the extremities began to be cold and the abdomen appeared to be "sunken in." One month later the mother noticed that the feet and hands began to swell. Since then cheeks and eyelids have also become swollen. This swelling has varied somewhat elsewhere, but has been constant in the feet.

The child has lost color only since the swelling appeared. Has passed urine very frequently. Bowels have been regular.

Examination showed a fairly well-developed and fairly well-nourished child. Skin and mucous membranes very pale. Anterior fontanelle, 1 x 0.5 cm.; four teeth. Rosary marked. Head of normal shape. No enlargement of epiphyses. Throat, heart, and lungs normal. Pulse rapid and of poor strength, 110 to 120; respirations, 27; temperature subnormal (97° F.). Urine, no albumin. Marked œdema of feet, hands, and face. Skin shiny and tense. On the left knee are two purpuric blotches, about 1.8 cm. in diameter. On the right side of the neck is a somewhat smaller area, similar in appearance. No glands are felt. Time of occurrence, June and July. End result unknown.

Case II.—E. B., boy, aged four months. Family and past history not obtainable. Examination showed a poorly developed and poorly nourished child. Skin pale and hanging in folds on arms and legs.

Anterior fontanelle, 2.5 cm. x 2.5 cm. Discharge from right ear. Glands in neck and groin not specially prominent. Heart negative. Lungs show few fine râles. Spleen not palpable. Liver 4 cm. below the costal border. Urine: pale, clear, slightly acid; specific gravity, 1005; no albumin, no sugar. The bowels were of the type of enterocolitis, with blood and mucus. For something over three weeks the temperature ran a type of moderate sepsis, never going below normal, and for most of this period above normal. On August 23d, however, it dropped suddenly from 100.8° to 97°, and on the following day œdema of the feet appeared. On the day after the appearance of the œdema the urine was normal, clear, strongly acid, no albumin, no sugar. Curiously enough, the pulse, simultaneously with the temperature, dropped to 80, while the respirations rose to 56. The lungs showed only the fine râles above mentioned. The œdema continued up to the time of death, which occurred suddenly nine days after its first appearance. The temperature on the day following its first drop to subnormal, rose to 100.4°. It remained normal or slightly above normal until five days before death, when it again fell to 97°, immediately rose again and at death stood at 99.2°, pulse 115, respiration 58. Post-mortem showed acute follicular enteritis, a few areas of bronchopneumonia, with atelectasis in the left lower lobe. All other organs normal except for their anæmic appearance. Time of occurrence, August 24th to September 1st.

Case III.—G. D., boy, aged four months. Always well up to two or three days ago, when diarrhœa began. Three days after entrance (six days after the beginning of the diarrhœa) œdema of the hands, feet, and face ensued. Temperature 102° F. Urine negative. This continued for four days, when signs of incipient meningitis supervened. Two days later meningitis was marked, and the child died in convulsions on the following day.

In this case during life there was no anæmia, no signs of rachitis, no loss of cutaneous elasticity, no signs of any organic trouble beyond the meningitis and the ileocolitis. Time of occurrence, September 1st to 13th.

Case IV.—R. G., girl, aged four weeks. Diarrhœa for three weeks. Examination shows a poorly developed and poorly nourished child. Fontanelle, 5 x 5 cm. All organs normal. After a subnormal temperature of three days œdema of the eyelids appeared. Urine normal; no albumin. No anæmia. Hæmoglobin 80 per cent. In fourteen days the temperature only once reached the normal, remaining persistently below the normal. The œdema disappeared before the child's discharge. She was otherwise doing well. Time of occurrence, August 10th to September 1st.

Case V.—G. S., boy, aged nine months. Family history: probably specific. One other child died from meningitis. Two others living and well. Child's bowels have been loose for some time. Examination shows a well-developed but poorly-nourished child. Skin coarse and scaling. Glands slightly enlarged in neck and groin. Heart, lungs, liver, and spleen negative. Hæmoglobin, 75 per cent. Urine: No albumin or sugar. Temperature subnormal on the thirteenth, fourteenth, and part of the fifteenth and sixteenth days, on which day œdema of the hands, eyelids, and face made its appearance. It increased until it became extremely marked in the hands and in the eye-

lids. Four weeks later it was still marked, especially in the eyelids. Now occurs an interesting note of the house officer: "During the night the child seemed to have difficulty in breathing. Acted as if there might be some laryngeal stenosis. Throat showed negative as far as could be seen." Death occurred the next morning. No post-mortem. Culture from the throat proved negative. Time of occurrence, August 16th to September 12th.

CASE VI.—A. M., boy, aged ten weeks; weight at birth, ten pounds. Fairly well developed, but poorly nourished. Skin and mucous membranes pale. Fontanelle, 5 x 4 cm. Organs normal, except bronchitis of slight degree. Urine pale; no albumin. After a diarrhœa of six weeks' duration œdema of the face ensued, lasting two days, with normal temperature. Two days later it again appeared, this time in the feet. Two days later it appeared again in the face and now also in the hands. A few days later the case was discharged by the closing of the hospital for the season. The œdema was still present. There was nothing peculiar about the temperature in this case. Time of occurrence, September 4th to 15th.

CASE VII.—L. U., boy, aged four months; weight at birth, four pounds. Premature, seven months. Fairly developed and nourished. Fontanelle, 2.5 x 2.5 cm. All organs normal. No anæmia. Urine: no albumin, no sugar. Vomiting and diarrhœa for six days before entrance, continuing less severe after admittance. Fifteen days after its onset (nine days after entrance) œdema of hands and feet appeared. Temperature 101°, pulse 102, respirations 35. On the following day the temperature rose suddenly to 104°, with slow, irregular pulse and modified Cheyne-Stokes respiration. König and Babinski signs on the left, with absence of the left knee-jerk. Delayed wink reflex. Just previous to death convulsive movements, at first irregularly bilateral, then left unilateral occurred. Unfortunately no post-mortem could be obtained. Time of occurrence, August 2d to 12th.

CASE VIII.—F. M., boy, aged eleven months. Well developed, poorly nourished. No teeth. Fontanelle, 5.5 x 5 cm. Epiphyses enlarged. Skin dry. Organs normal. The child has had pneumonia twice, five months and one month ago. For delayed convalescence from the last attack he is sent to the hospital. The movements from the bowels were somewhat frequent and contained mucus. Repeated examination of the urine showed negative results. He refused feedings, and was, therefore, fed by tube. Beyond this he did well until three weeks after entrance, when the stools became foul, and two days later œdema of eyelids was noticed, soon extending to cheeks. The right eye could not be opened. With some fluctuation in severity it continued to a day or two before death, when it began to diminish, but was still present in the eyelids. Temperature fluctuated between 96° and 101°. Its average was far below normal. On the day of the appearance of the œdema it was normal. At death it was 96°. Post-mortem: Slight ileocolitis; heart, lungs, and kidneys normal. Time of occurrence, August 7th to 13th.

CASE IX.—L. H., girl, aged three months. Nursed four or five days, since then has been given condensed milk. Two days before entrance diarrhœa began; green, slimy, no blood, ten times daily. Occasional vomiting. Examination showed a well-developed but poorly nourished child, with no evidence of organic disease and no anæmia.

Red corpuscles, 4,528,000; white corpuscles, 13,500; hæmoglobin, 95 per cent. Urine negative. While in the hospital the movements were much less frequent than above stated by the mother; yellow and green, with occasionally a little mucus. Eight days after entrance a slight purulent discharge from the right ear occurred. Sixteen days after admission œdema of the right side of the face occurred. Temperature normal, pulse 110, respiration 30. Œdema became general and finally completely closed both eyes (see Fig. 1). It was not limited to the extremities and face, but was marked also on the back and chest. It

Fig. 1.

was specially marked, however, on the dorsal aspect of the feet and hands, on the sides of the face, and top of the head. Slight ascites was noticeable. Nine days after its onset it had increased to extreme degree, then for a day seemed much less marked. On the following day, however, it was again very marked. Thence on it fluctuated considerably in intensity and distribution until death, seventeen days after its onset. The second photograph shows well the œdema of the dorsum of hand and fingers. The œdema of the chest is also indicated

Fig. 2.

in this photograph by the apparent plumpness of the thorax compared with the emaciated upper arm. For the solicitude with which the baby is kept covered is responsible one of the most interesting features of the case. This was persistently subnormal temperature. One week after the appearance of the œdema the temperature fell to subnormal, reaching on four different occasions as low as 95° F. and standing at death at 94° F. Only twice in twelve days did it touch the normal, and then only briefly. Toward the latter period of its illness the child showed visible evidence of anæmia.

Post-mortem, twenty-two hours after death: no œdema of the brain; sinuses filled with fluid blood; no thrombosis; pleural cavities contain 200 c.c. of serous fluid; no adhesions; pericardium contains 12 c.c. of similar fluid; otherwise normal. Peritoneal cavity contains 400 c.c. of serous fluid, but shows nothing otherwise abnormal. Lungs, bronchopneumonia. Heart, liver, pancreas, spleen, and kidneys show nothing abnormal. Pelvis and ureters normal. Thymus rather large. Gastrointestinal tract presents no marked lesion. Time of occurrence, August 20th to September 6th.

Before considering these cases in detail it will be of interest to add certain other, seemingly analogous, instances reported by other observers. By thus enlarging our material we may obtain a more accurate average on which to base any conclusions we may wish to draw. The writer has taken the liberty of selecting from the reports that have come under his observation only those cases that can without question be included in the class with which this paper is to deal, namely, those in which there is no evidence of organic disease of the heart or kidneys, or chronic disease of the lungs, or possible congenital anomaly of the vessels, or local obstruction of the same. A few cases are thus omitted which might perhaps be included were the writer in possession of more accurate data concerning those individual cases. Here, also, it must be explained that it has seemed best to regard albuminuria as cause for the rigid exclusion of a case. Several cases have been reported, however, in which œdema was accompanied by albuminuria, in which the autopsy showed no evidence of nephritis.

Cases of œdema occurring in the course of or following contagious diseases, of which a number of instances have been reported, will be mentioned elsewhere.

Girl, aged twenty-three months (Morse'). Œdema of left arm and hand, with pitting. No known injury or exposure. Otherwise well. Surface slightly reddened and somewhat hot. No tenderness or pain. Arm freely used. Four days' duration. No recurrence. Time of occurrence, March.

Girl, aged seven months. Œdema of both forearms and hands without pitting. Following a cold bath. Otherwise well. Surface shiny, cool, not tender. No restraint of motion. Two days' duration. Return a few weeks later after sleeping in a cold room. Duration two weeks. Gradual disappearance. Recurrence after exposure to cold the balance of the winter and spring, lasting from a few hours to a day at a time. No recurrence the following summer or winter, but return the winter after on exposure to cold air in October.

Girl, aged four months. Since birth attacks of œdema of right arm, without pitting. No known injury. Surface during attacks warm, purple, not tender. Some restraint in use of arm. Axillary glands not increased. Otherwise well. Occurs any time of day or night. Duration, two to six hours. Less in warm weather, more frequent in cold.

Child, aged six days (De Wolf[2]). Œdema of feet, arms, legs, and face, lasting seven days. Heart and urine negative. No record of condition of bowels. Child discharged in fair condition with no œdema.

Boy, aged ten months. Œdema of face, hands, and feet, lasting about three weeks. Heart negative. Urine 1008; no albumin. Blood examination: hæmoglobin, 60 per cent.; red blood corpuscles, 2,972,000; white blood corpuscles, 11,400. Temperature subnormal. Child had suffered for weeks with a gastroenteritis. Two weeks after its disappearance the œdema again appeared in the hands and feet, and later in the face and prepuce. Urine negative. Death four weeks later. Post-mortem: All organs normal. Diplococcus obtained by culture from organs, but not from heart. Microscopic examination of organs negative.

Child, aged nine days. General œdema, so far as known, of about one week's duration. A systolic souffle of transient character was heard in this case. Child had enteritis. End result unknown.

Girl, aged three months. General extreme œdema. Heart, lungs, and abdomen negative. Urine, no albumin. Gastroenteritis. End result unknown.

Child, aged twelve days. Œdema of face, feet, and hands, also of glottis apparently, lasting five days, with intercurrent pneumonia and death. No bowel disturbance. No post-mortem.

All of the children were anæmic and generally with subnormal temperature. In three other cases, six weeks, eight months, and one age unknown, respectively, with similar signs of marked œdema, albuminuria was present without any sedimentary evidence of renal disease. In two of these cases post-mortem examination also failed to show any organic change. In the six-weeks-old child microscopic examination of the kidneys showed no disease. These cases are noted as a matter of general interest, but will not be included in the final consideration.

Four children, aged from six weeks to two and a half years (Cassel[3 4]). General marked œdema, in three instances combined with ascites, occurring in children without previous evidence of contagious disease, without affection of the heart, and with urine showing neither albuminuria nor sedimentary evidence of renal disease. Three of these cases had intestinal disturbance preceding the occurrence of the œdema. The other was otherwise perfectly well. Repeated examinations of the urine, frequently several times a day, failed to show the presence of albumin, although the exceedingly delicate ferrocyanide test was used. Microscopic search for renal elements was also without result, although the centrifuge was employed.

Girl, aged seventeen months (Variot[5]). Marked œdema of eyelids, thighs, legs, and hands. Heart sounds normal. No albuminuria. One week later rapidly diminished. No explanation could be offered by the author.

Boy, aged twenty-three months (Griffith and Newcomet[6]). Dropsy of eyelids, hands, feet, and abdominal cavity, beginning five weeks previously with fever, diarrhœa, cough, and cold extremities. Heart, lungs, and urine negative. Liver enlarged. Extension of the œdema on following day to left lower extremity, with fluid in right pleural cavity. Dyspnœa, cyanosis, and general malaise. Still no albuminuria. Blood. Hæmoglobin, 65 per cent.; red blood corpuscles, 3,500,000. Discharged cured two months later. Unexplained.

Girl, aged two years (Rilliet and Barthez[7]). Œdema commencing in the extremities and becoming general, with gradual development of ascites. Child delicate, but well up to appearance of this condition. It was with difficulty that the child was kept warm. Urine contained no albumin, and the sediment showed only pavement epithelium and mucus. Heart negative. Skin pale. No temperature. This condition continued some time, with some alterations in intensity, then diarrhœa ensued. The skin was frequently covered with perspiration. No temperature. After a succession of increase and decrease in the dropsy, absorption began, with gradual amelioration of the general condition. At time of discharge, three months and one week after onset, the œdema was almost entirely gone. Repeated examination of the urine for albumin and sediment were all without result.

Girl, aged two years (Churton[8]). General anasarca without albuminuria or any discoverable cause, lasting three months, with recovery. Patient alive and well twenty years later.

Boy, aged two years (Seilikovitch[9]). Œdema of the hands and left foot, of slow onset and long duration. Chemical and microscopic examination of the urine negative. Child had diarrhœa for five or six weeks.

Girl, aged eleven years (Markow[10]). Acute œdema of the face and extremities, following severe mucous diarrhœa. Some ascites. Heart negative beyond a faint souffle at apex. Liver and spleen somewhat enlarged. Urine 1003 to 1005, containing no albumin or organic elements, although many examinations were made. Child poorly nourished and anæmic. Recovered in a short time.

Boy, aged five years. General œdema which on entrance (two days after the preceding case) had lasted two weeks. Heart and lungs negative. Liver somewhat enlarged. Urine: no albumin or renal elements, 1003 to 1004. For five weeks he had suffered with severe diarrhœa. Child poorly nourished and anæmic. Like the other case, he recovered in a short time.

Boy, aged eight years (Filatow[11]). General œdema. This child also had preceding intestinal catarrh. Otherwise no disease.

Boy, aged six years (Loimann[12]). Œdema of eyelids, cheeks, and lips, and once involving the genitals, lasting three or four hours, without other disturbance or organic lesion of any kind. Child in good general health. During the last few months also seemed to involve the pharynx, with difficulty in swallowing, disappearing in three or four hours. These attacks continued over the three years during which the child was under observation.

Boy, aged four years (Goodhart[13]). General dropsy, with ascites and possible pleural effusion. All organs normal. Urine 1007. No albumin on repeated examinations. No history of contagion. Nine days previously he had a sudden attack of vomiting.

Girl, aged four years (Henoch[14]). Œdema of face and dorsum of feet. A few days previously had stood by an open window for some time, on a very cold day. The œdema appeared on the following morning. Anorexia, light fever and some pain in the feet. All organs normal. Urine scanty and urates precipitated. No blood. No albumin. Recovery in three days.

Girl, aged four years. Œdema of face, hands and feet, recurring three or four times in a few months; each time lasting a week and

accompanied by general malaise and once with vomiting. Repeated examinations of urine and organs showed nothing abnormal.

Child, aged four years. Œdema of face and thighs. Otherwise well. Urine light colored, large in quantity, no albumin. No cause whatever found. Recovery in twelve days.

Boy, aged nine years. Œdema of face and genitals. Child in good condition and perfectly well otherwise. Urine negative in all respects, although repeatedly examined. No cause could be discovered. Well in three weeks.

Girl, aged nine years (Mooney[15]). Œdema of hands. Child anæmic and poorly developed. Occurred in course of gastrointestinal disturbance.

Girl, aged five and one-half years (Wagner[16]). Œdema of face and legs, increasing thence to entire body, with slight ascites. In face so extreme that eyes and mouth were closed. Duration when first seen eight weeks. Child pale, temperature normal. Heart and other organs normal. Urine 700 c.c., 1009. Repeated search failed to show either albumin or renal sediment. Three weeks later diarrhœa ensued. Six weeks later cough. Otherwise well. When a year old she is said to have had a similar attack after vaccinia.

Boy, aged twelve years. Œdema of lower and upper extremities, face, back, and scrotum. Skin moderately pale, cool, slightly moist, elastic. No venous distention. Glands not enlarged. No rachitis. Heart and lungs normal. Urine small in quantity, 1016, color dark. Repeated examination failed to show albumin or sediment. Temperature 36.8° C. Pulse 80, normal. Appetite, sleep, and bowels unaffected. His only complaint is "heaviness in legs." Poorly nourished, moderately pale child. His mother is said to have died "of dropsy." Scarlet fever, diphtheria and pertussis in his third year. In his eighth year suddenly, and without evident cause, swelling in both legs occurred, lasting three weeks. In his ninth year a similar occurrence, this time involving the upper extremities slightly also. In his tenth year again occurred, this time in face also. In his eleventh year repetition of the same affection. Each time lasting about three weeks and each time occurring in the summer.

Child, aged three years. General dropsy of moderate degree, lasting for several weeks, with extreme marantic condition. No cause evident. Heart and kidneys normal.

Boy, aged fourteen months. Œdema of legs and arms, soon extending to entire body. Child previously always well. Heart and kidneys normal. Urine sediment contained only an occasional red and white blood corpuscle. Pulse small and increased in rate. Temperature 34.9° C., and remained persistently subnormal. Bowels normal. Death occurred three months after onset, and just before death a few casts appeared in the urine. Post-mortem: General œdema and marked anæmia. Heart, kidneys, and spleen were normal. The other organs, including the brain, were œdematous and anæmic, except the lungs, which were not œdematous, but showed pneumonia in one or two lobules. One other child in this family was lost by dropsy of unknown origin.

Boy, aged four years. General œdema of moderate severity, especially severe in face and genitals, with hydrothorax and ascites. No evident cause. Heart normal. Urine: no albumin, 1019. Bowels normal. Temperature 37.6° C. Child not strong, and very pale.

Five weeks later, with œdema continuing, diarrhœa ensued, two or three times a day, with blood and mucus. This soon increased in severity and frequency, while the œdema diminished and finally disappeared except on the legs. Six days later, or forty days after onset of the dropsy, death, preceded by convulsions of entire body, and occasionally of face alone, occurred. Post-mortem: Few pneumonic lobules in right lung. Heart, kidneys, spleen, external and internal lymph glands and muscles, all normal. The thymus could not be found. Liver showed many "small red atrophic areas." Uniform injection and swelling of the colon, with occasional shallow ulcerations.

Boy, aged two months (Biedert[17]). Œdema of face and extremities. The author speaks of the case as "hydrops hydræmicus."

Boy, aged seven years (Torti and Nazàri[18]). General œdema. Began in face. Heart, lungs and kidneys normal. Cyanosis with dyspnœa supervened five months later, and death occurred. Post-mortem: Kidneys normal. Heart dilated, otherwise normal. Lungs showed old pleurisy, but were otherwise negative. Bone-marrow showed some change. Red blood corpuscles, 5,000,000; white blood corpuscles, 20,000 to 24,000; hæmoglobin, 75 to 85 per cent. The interesting condition referred to in the title concerns the microscopic examination of the blood. Macrocytes and microcytes. A number of globules showing evidence of polychromatophilic degeneration. Mononucleated and polynucleated megaloblasts. Very numerous nucleated red corpuscles. About 1 to 200 of ordinary reds.

Boy, aged eight years (Widowitz[19]). Œdema of face and hands for two years in recurrent attacks, apparently excited by exposure to cold air. No subjective symptoms or organic lesion. Urine, 1014; amount 1250 c.c.

Boy, aged six years. Œdema of face and hands after exposure to cold. No organic lesion. Some itching accompanied the attack. Both of the children were anæmic.

Girl, aged seven years (Widowitz[20]). Œdema of nose, cheeks, and fingers. Attacks since her fourth year.

Boy, aged eight years (Graham[21]). Œdema of eyelids, face, and feet, more marked on the left. Attacks have occurred since one year of age.

Girl, aged two years (Griffith[22]). Œdema in upper extremities and face. Attacks associated with urticaria and constipation.

Boy, aged eight years (Masterman[23]). Œdema of "wandering" character, acute and involving face and entire body before it ceased. Lasted two weeks, and was followed, after a few days, by dysentery of great severity. Swelling was extreme and did not pit. Urine negative.

Boy, aged fourteen years (Schlesinger[24]). Œdema of lids and nasal mucous membrane, occurring on nervous excitement and attended by headache and occasional vomiting without nausea.

Girl, aged five years (Johnston[25]). Œdema of hands and feet, occasionally of hands alone, or ears, nose, hands, and feet. One to six attacks a day, induced by cold, also at times apparently by nervous excitement. Accompanied by reddening, pain, and lowering of local temperature. She had similar attacks when three months old.

Girl, aged fifteen years (Simon[26]). Œdema of hands, forearms, feet, legs, and face, reaching its maximum in fifteen minutes, lasting one to

four days. Perfectly well subjectively and objectively during the attacks. These attacks had recurred ever since she was five years old. Urine light in color. No albumin. No casts.

Boy, aged two and one-half years (Rotch[27]). Œdema of eyes and cheeks. Recurrent attacks since age of nineteen months, occurring each time about fifteen minutes after eating some egg.

Boy, aged three years. Œdema of fingers and dorsum of hands. Recurrent sudden attacks, ceasing after operation for phimosis.

Boy, aged fourteen years (Ashton[28]). Sudden œdema of right eye and surrounding tissues following twenty-four hours after a fall in which he struck on this region. This lasted fourteen days, then terminated as suddenly as it began. This was in the morning. In the evening it suddenly appeared in the left eye, etc., lasting two days, and suddenly vanishing. No subjective symptoms. No organic lesion. No disturbance of stomach or bowels.

Girl, aged four and one-half years, and girl, aged three and one-half years (Gaillard[29]). Two cases of acute palpebral œdema, lasting from twenty-four to forty-eight hours, without organic lesion. Urine negative. In one case eight relapses occurred. The other was preceded by rheumatism, with effusion into the right knee-joint a week previously, and by an erythema of the lower extremities two days before, and followed by a purpuric eruption on thighs and nates.

Girl, aged five years (Trousseau[30]). Quotes Andrieux, who mentions a girl who was afflicted with recurrent attacks of œdema of the eyelids lasting two to four hours, without known cause.

Girl, aged three years (Gevaert[31]). Child of nervous temperament, but otherwise well. Œdema of left side of neck occurring about every fifteen days. Origin unknown.

Boy, aged eight years (Josephs[32]). Œdema of exposed parts. A similar case in this boy's cousin, a boy of five years, is here omitted on account of the child having been subject to paroxysmal attacks of hæmoglobinuria.

Boy, aged seven years (Falcone[33]). Acute œdema, in which hereditary predisposition existed, the grandfather having had similar attacks.

Boy, aged one year (Dinkelacker[34]). Attacks of localized œdema from the third month.

Boy, aged nine years (Hamburger[35]). Œdema of lower extremities and genitals, with ascites and pleural effusion. Duration three months. He isolated from the ascitic fluid a bacterium which he considers a causative factor.

Girl, aged fifteen months (Durando Durante[36]). Child developed œdema of face and lower extremities, with intestinal disturbance. Poorly nourished, pale, emaciated, and rachitic. No teeth. Blood: hæmoglobin, 45 per cent.; red blood corpuscles, 5,050,000; white blood corpuscles, 18,120. No lesion of the heart or kidneys. The author considers the œdema probably the result of toxæmia from intestinal infection.

Boy, aged four years. General œdema, commencing in legs and face. Intestinal infection. Enteritis. Pale and emaciated. Blood: hæmoglobin, 35 per cent.; red blood corpuscles, 3,430,000; white blood corpuscles, 6246. Recovery in fifteen days. No lesion of heart or kidneys. Child had "bronchopneumonia" while œdema was present, apparently without effect upon it. Virulent (for guinea-pig) culture of bacteria lactis aërogenes, Escherich, was isolated from the stools.

Children, two to six years (Guidi[37]). Four cases in children from two to six years of age in whom clinical examination revealed no other cause for the œdema than the presence of a number (30 to 40) of ascarides, and in one case also oxyuris in the intestinal tract. Duration, fifteen to forty days. The author thinks that the œdema was caused by the action of the products of the excretion or secretion of the worms acting on the central nervous system or on vessel walls.

Boy, aged five and one-half years (Griffith and Newcomet[6]). Rash on back and abdomen, with few urticarial wheals. Rash assumed a purpuric character, with general erythema and urticaria and extreme œdema of the face. All disappeared in two days. Repeated examination of the urine showed nothing abnormal.

Boy, aged two and one-half years. A month ago red blotches began to appear on various parts of the body, lasting only a few hours in any one spot, and followed by œdema. At present child is emaciated and anæmic. Heart, lungs, and urine, on repeated examinations negative. Œdema of right hand, forearm, right leg and foot of four days' duration. Glassy and pitting. Temperature 99.2° to 100° F. Bowels loose and green from three weeks after onset to present.

Girl, aged two and one-half years. The following case, seen by the writer in private practice, will add another to the list. During the course of the day the mother noticed that the hands and feet seemed larger than usual. When seen by the writer in the evening there was extreme dropsy of eyes, face, hands, and feet, and the entire body was considerably swollen. Over the upper portion of the left thigh was a profuse eruption of typical urticarial wheals over an area the size of an average hand. Over the corresponding portion of the right thigh were a few scattered wheals. The skin was exceedingly tense, very shiny, and no pitting could be anywhere produced. There was no evidence of any organic lesion, and the urine was normal in every respect. Beyond severe itching there was no subjective complaint whatever. Temperature, 99.5° F. Pulse and respiration perfectly normal. Bowels constipated. Movement from the bowel the next morning, following a laxative, brought away a mass of semidecomposed material, the nature of which could not be ascertained. All of the above phenomena disappeared before the following day.

These cases show how wide may be the range of this affection over the period of infancy and childhood; how varying within certain limits the clinical symptoms themselves may appear, yet how striking is the presence of the predominant characteristic of the affection—dropsy—with normal heart and kidneys, organs usually so closely associated with the production of dropsical conditions.

To these 72 cases may be added 42 cases reported by Rilliet and Barthez,[7] and 50 or more cases mentioned by Holt.[38] Moisson,[39] who has reported 46 cases, was interne on the service of Barthez in the hospital of Sainte-Eugénie. It is, therefore, unfortunately impossible to tell how many of these cases have been included in the above 42. We can only add the 4, by which number his cases exceed those of Rilliet and Barthez. This gives us a total of more than 168 cases of this affection that for convenience we have termed "essential" dropsy.

This is exclusive of all cases occurring with or closely following any of the ordinary infectious diseases. These cases are all in children under fifteen years. Of the 72 cases we have collected, 60 were in the first half of this period, namely, under eight years, or 83 per cent. of the total. Of the remaining 12 cases, 4 have a history of previous attacks in earlier life, which would also place them in that period, if these histories are correct, and would give us a percentage of 88.

Of those whose sex is stated, 59 per cent. were boys, 40 per cent. were girls. The time of year has, in the writer's opinion, an influence on its occurrence only in so far as the seasons are accompanied by those factors that are of undoubted importance in the etiology, such as extremes of temperature, especially cold, or the prevalence of gastro-intestinal derangements, with their accompanying toxæmias and conditions of low vitality.

In 25 per cent. of the cases anæmia is definitely stated to have been present. In 43 per cent. there was gastric or enteric disturbance; usually diarrhœa. In 15 per cent. there was emaciation of marked degree. In 15 per cent. the temperature was subnormal. In a few cases it was about normal. Urticaria was seen in about 7 per cent., purpura in 4 per cent.

Symptoms suggestive of œdema of larynx or throat occurred in 5 per cent. In 2 cases symptoms attributed to meningitis may possibly have been due to cerebral œdema. Unfortunately, in neither case could a post-mortem be obtained.

In considering the mortality the age of infancy should, we think, be considered separately, since the mortality is much greater during this period than later in childhood. In the cases under two years the mortality was 34 per cent. This is not nearly as high as has been thought. A number of these cases died of intercurrent disease. In the cases two years and over, death occurred only twice, a mortality of slightly over 4 per cent. The difference in mortality between infancy and childhood is due not so much to the œdema as to the low state of vitality in infancy, and especially of those cases in which œdema is likely to occur. It should be constantly in mind, however, that the affection, at any time of life, is not devoid of danger. Several cases of sudden death in adults have been reported.

The association of anæmia, marasmus, and subnormal temperature with this affection is also chiefly confined to the first two years of life.

In the 9 cases who were under two years, reported by the writer, anæmia was present in 44+ per cent.; but in half of these it did not appear until after the œdema. The temperature was subnormal in 66+ per cent. of these cases at some time during the affection, but in only 2 cases persistently so. There was diarrhœa in 77+ per cent.

Of all the abnormal features that may be found associated with

"essential" œdema, far the most common is some disturbance of the gastrointestinal tract. This may, in a small percentage of cases of the very acute form, be due to a coincident affection of the mucous membrane, similar to that of the skin, but in the great majority of the cases it is probably an antecedent affection, often of great importance in the etiology of those cases of œdema in which it is present. Cyanosis is not a characteristic feature of the affection.

The cases of Rilliet and Barthez are not considered in detail, and the only summary given, that of age and sex, and time of year, includes also the infectious diseases, which makes a comparison impossible with these 72 cases, none of which were in connection with any contagious disease. Much the same is true of the cases of Moisson. Holt mentions that over 50 cases have been observed in the Babies' Hospital, but the details, so far as we know, have not been published.

In 1882 Quincke[81] described an affection which he called "acute circumscribed œdema of the skin," and which he regarded as an angioneurosis, having the following character: œdematous swellings of the skin and subcutaneous tissues, appearing over multiple areas simultaneously, reaching their maximum in a few hours and rapidly disappearing, after an average duration of about a day, with rarely any disturbance of the general health, and never any temperature.

It is clearly evident that Quincke's cases were one form of the affection we have here under consideration, and that they belong in the first class, which, for convenience, until some better classification shall be devised, we will consider those without other disturbance in the general health.

Strübing,[82] in 1885, reported some cases apparently of much more severe character and associated with some subjective disturbance and intercurrent attacks of vomiting.

That the affection is of nervous origin is the opinion of the two observers above quoted and of the great majority of those who have since reported cases both in children and adults, or who have described the affection without mention of cases. Among these are Widowitz,[20] Rilliet and Barthez,[7] Simon,[26] Elliott,[83] Collins,[84] Bauke,[85] Bircher,[86] Fuchs,[87] Sachs,[40] Senator,[88] Feré,[89] Oppenheim,[90] Mooney,[15] Baruch,[91] Griffith and Newcomet,[6] Lodor,[92] Schlesinger,[93] Laudon,[94] Onuf,[95] Kohn,[96] Madinos,[97] and others, and most of these regard it as a vasomotor neurosis.

The character of the majority of these cases was acute. We must bear in mind, however, that it is not by any means always so; that it may be subacute both in its onset and in its course, as many of our cases show; and that forms have occurred of so long continuation as seemingly to almost justify the term chronic. Whether the famous cases of Milroy,[98] and the equally interesting but less known instances

reported by Meige,[99] should properly be included in the class of cases we are considering is very doubtful. Milroy states, however, that his cases were considered by Welch to be of angioneurotic origin, and that Osler concurred in this opinion. Here it may be of interest to refer to certain affections that are probably allied to our cases.

Of great interest are the instances of intermittent hydrops of the joints, of which a number of cases have been reported. Pierson[41] reports the case of an eleven-year-old girl who for two years was affected with sudden painful swelling of various joints without evident cause and who was otherwise perfectly well. Among those who have described this affection are Schlesinger,[24] Moore,[100] Köster,[101] and Feré,[89] who regard it as an angioneurosis. Senator,[88] in a comprehensive article on the subject, also considers it a disturbance of vasomotor character.

Quincke,[42] in 1882, reported 6 cases of ascites in girls of eleven, twelve, and thirteen years, of gradual onset, without any marked general disturbance beyond, in one or two instances, transient fever, vomiting, and loss of appetite. In 4 cases rapid disappearance occurred with the onset of the menses. Otero[43] (Mexico) described a form in which the abdomen is distended, the face, eyelids, hands, and feet are œdematous. "It occurs in its full development in children between the ages of two and one-half and fifteen years, but occurs, in its milder forms, in nursing infants as well as adults." The disease was preceded in almost every instance by a long period of diarrhœa. Urine and all organs were normal, and post-mortem examination on the fatal cases showed no organic disease beyond dilatation of the stomach. Ferron,[44] in a thesis published in Paris in 1902, gives a comprehensive account of acute œdema of the eyelids in young persons. Another excellent account, although dealing with adults, is that of Fuchs,[87] who considers it an angioneurosis. Ferron also considers the neurotic element, although he also thinks it may be "rheumatic or gouty."

Œdema Neonatorum. This is an œdema, more or less general, coming on usually in the first two or three days of life, or at least within the first two weeks, in weakly and often premature infants. It is a rare affection. The lower limbs and lower portion of the body are the usual locations of the dropsy. Parrot,[45] Klebs,[46] Dumas,[47] Ballantyne,[48] Henoch,[49] Semet,[50] Pontiacaccia,[51] and Audebert[52] are among the writers on this subject. Semet considers it due to weakness of the right heart, with deficient inspiratory power and consequent venous distention. Several of the cases reported were congenital. Œdema neonatorum has been confused with scleroma neonatorum, but the two affections are not allied.

In œdema the skin is usually soft; it may or may not pit; it can be pinched up in folds, unless the œdema is extreme; rigidity of the body

is not present; the skin when cut at autopsy exudes serum, and when examined under the microscope large spaces are seen where the connective tissue has been forced apart by the fluid.

In sclerema the skin is hard, in severe cases as if frozen; it never pits; it cannot be pinched up, but seems as if it were fastened down to the underlying parts; there is more or less rigidity of the entire body; there is no exudation of serum when the skin is cut; and when examined in section it and the subcutaneous tissue is seen as a dense mass in which fibrous tissue predominates and no dilated interconnective tissue spaces are present.

The only way in which the two affections are similar is that they both occur in feeble and often premature infants in the first few days of life.

Interesting are those cases of dropsy without evidence of heart or renal disease occurring after the infectious diseases. Such cases following scarlet fever are mentioned by Philippe,[53] Quincke,[54] Thomas,[55] Goodhart,[13] Henoch,[56] Senator,[57] Rilliet and Barthez[7] (p. 109), Steiner,[58] Duckworth,[59] Roberts,[60] Maestro,[61] Moisson,[39] Gee,[62] Niemeyer,[63] Hillier,[64] and Rosenstein.[65] There can be no doubt but that such cases occur absolutely without involvement of the kidney, but the observations of Fenini[66] and Litton[67] teach that great caution must be observed in each and every instance before such is assumed to be the case.

Senator thinks that in these cases the vessels of the skin are injured independently of the kidneys.

Moisson[39] reports 5 cases after measles, Rilliet and Barthez[7] 2, Giarré[68] 1, Cassel[3] 1, and the writer considers Galatti's[69] case also in this class.

Cassel,[3] Wagner,[16] and Stark[70] report cases after varicella. Stoeber,[71] Rilliet and Barthez,[72] Henoch,[73] Stembo,[74] Moisson,[39] and Cadet de Gassicourt[75] all mention cases in the course of typhoid; the latter author citing 14 cases occurring from the ninth to the fortieth day and lasting from eight to thirteen days.

Manifold causes have been regarded as the etiological factor in the causation of these so-called essential dropsies. This has caused much confusion and great difference of opinion on the subject.

No one condition has been more generally considered a cause perhaps than anæmia, unless it is exposure to cold. In many of the textbooks the only mention of any such œdema is the brief statement that it occurs in anæmia. But authors who have considered the subject much more thoroughly, as Holt,[76] Griffith,[6] Henoch,[77] Donkin,[78] and Houston,[102] etc., also consider anæmia of etiological moment. The first four of the above writers also regard a marantic condition in the same relation. Rilliet and Barthez,[7] Moisson,[39] Basham,[103] Taylor,[104] Lascols,[79] and Frerichs all hold that exposure to cold is the chief factor.

In many of the cases cited in this paper the same opinion will be noticed.

Frerichs considered such cases as due to paralysis of the cutaneous nerves from cold.

Filatow,[11] Lassar,[105] Masterman,[23] Durando Durante,[86] Herringham,[80] and others consider these œdemas of toxic origin.

Bircher,[86] Ashton,[28] and Strübing[82] report cases where trauma seemed to be a cause. Rotch's[27] case seems to point to certain food, Kerley's[106] and Oppenheim's[107] to drug idiosyncrasy as a cause. Guidi's[37] cases were apparently due to intestinal parasites. Emotional causes have also been noted. That heredity may be an apparent element in the etiology we know from the well-known case reported by Osler.[108]

Thus we see in studying the literature that the causes are apparently endless and the etiology considerably confused. In the writer's opinion this confusion is due to the fact that each of these factors enumerated has been regarded as the direct and primary cause of those individual cases. If now we divide these different factors on the basis of the theory that there are two conditions concerned in the etiology of this affection, the whole subject becomes much simplified. In other words, there must be first a predisposing then an exciting cause.

The writer believes that in the great majority of cases this affection is produced by a reflex sympathetic disturbance having its origin in a direct exciting cause, acting on any portion of the sympathetic system, but producing its effect through the terminal filaments in the vessel walls. This exciting cause, provided it be sufficiently severe, may in itself alone evolve such reflex, even in a normal condition of the nervous system, but there is usually a predisposing condition antedating the action of the exciting cause.

As predisposing causes we consider anæmia, marasmus, including subnormal temperature, and heredity. As direct exciting causes we may consider toxic, chemical, including the action of food or drugs, extremes of temperature, especially cold, trauma, peripheral irritation, and psychical disturbance.

Urticaria and other skin affections are to be regarded as merely accompanying phenomena, the effect very probably of the exciting cause of the œdema, but not its cause, as has been thought by several writers, as Courtois-Suffit.[109] That extreme irritability of the nervous system frequently exists in anæmia, marasmus, and allied states of low vitality is a well-known fact.

It is especially true of the age of infancy and childhood. Such children are extremely irritable, crying at the lightest touch, starting at the least noise, reacting to causes to which a normal child is wholly indifferent. Such a child sleeps in the lightest degree of unconsciousness, starting at the slightest noise or touch, reminding the writer

often of the extreme sensitiveness of white mice, with which every bacteriologist is familiar. It is incidentally an interesting fact that this supersensitiveness of mice is sometimes greatly intensified by disease, especially toxæmia from bacterial infection.

It is conceivable that, the sympathetic system participating in such a condition of unstable nervous equilibrium, any irritation, peripheral or central, external or internal, might be sufficient to overthow its balance. In fact such an occurrence in childhood in connection with the production of reflex-phenomena is a matter of common experience.

That œdema may be produced by nervous action is evidenced by the experiments of Ranvier,[110] Ostroumoff[111] and Gergens;[112] by the occurrence of œdema simultaneously with phenomena of undoubted nervous origin; by the occurrence of local œdema in association with local neuralgic attacks; and by the fact that different and widely separated parts of the body are often simultaneously affected, and that occasionally absolutely symmetrical areas are involved. Whether the transudation is brought about by an irritation of the vasodilators or by a paralysis of the vasoconstrictors, or whether it is the stimulation of secretory function must remain a question for future experimental physiology to answer.

It seems probable that in a large proportion of the cases with gastro-intestinal disturbance that the reflex impulse has its origin in the terminal sympathetic fibres in the walls of the intestines or stomach. In a few cases toxic or chemical irritants may perhaps be absorbed and act directly on the vascular terminal filaments of the sympathetic or upon the central nervous system.

The affection is probably always secondary in the sense that it is induced by an exciting factor, often favored by inherited or acquired predisposition; and is "essential" or "idiopathic" only in the sense that it is not caused by disease of organic nature.

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NEPHROPEXY IN A CASE OF CHRONIC NEPHRITIS.

BY J. NORMAN HENRY, M.D.,
OF PHILADELPHIA.

J. S., aged twenty-four years, laborer.

Family History. Father living and well. Mother died of "consumption of the stomach." Two uncles died of Bright's disease.

Past History. Had usual diseases of childhood. Acute inflammatory rheumatism five years ago, which disabled him for one year. Has not had a second attack. Had typhoid fever four years ago. Had "some fever" in Philippine Islands which kept recurring at frequent intervals during his stay there (malaria?). Uses alcohol steadily, but not to excess. Denies any venereal infection.

Present Trouble. About two months ago, face, abdomen, arms, and legs began to swell. Became very short of breath. About six weeks ago began to have trouble with vision, things appearing blurred, and being unable to read. Has had a good deal of headache. Had some nausea and vomiting. Appetite has been good. Bowels move two or three times a day. Urine has lately increased in amount (patient getting up two or three times during night to urinate), and is of a pale yellow color. Skin has become paler. Œdema has decreased somewhat lately.

Physical Examination. Temperature, 98.4°; respiration, 28; pulse, 80, of fair force and volume. A well-nourished young man, of anæmic appearance. Skin and mucous membranes pale. Tongue moist and clean. Face puffy. Considerable œdema of legs and thighs. Penis moderately œdematous, scrotum markedly so. Arms and trunk slightly œdematous. Lungs: slight impairment at right base. Breath sounds everywhere faint, but especially so at right base. Heart: dulness third rib, right border of sternum, four inches to left. Apex in fourth interspace nipple line. Faintly palpable apex-beat. Sounds about normal. Aortic second sound markedly accentuated. Liver: dulness in midclavicular line extends from fifth rib to costal margin. Abdomen: flat, soft, no dulness in flanks. Urine: opaque, pale yellow, slight flocculent sediment, acid, 1009, no sugar, large quantity of albumin, many hyaline and granular casts and epithelial cells, some leucocytes and red blood cells, degenerated cells (granules on casts and degenerated cells stain black with osmic acid).

Ophthalmoscopic Examination by Dr. Harlan. Extensive white patches of degeneration involving macula lutea in both eyes. Several punctate hemorrhages in right eye. Says vision is poorer than on admission. Cannot read at all, and cannot recognize objects or persons at a distance of more than one or two yards. Seems slightly more œdematous.

Examination of twenty-four hours' specimen of urine (1725 c.c.); urea, 1 per cent. or 17¼ grammes; albumin, 0.3 per cent.

May 31st. Complaining of considerable headache this morning. Perspires freely in hot-air baths, and until this morning had felt somewhat benefited by them.

June 5th. Has had a good deal of pain in eyes past few days. Vision is no better. In other respects patient says he feels much better. Œdema is considerably less marked than on admission. Blood: erythrocytes, 3,723,000; leucocytes, 11,800; hæmoglobin, 63 per cent.

8th. Examination of twenty-four hours' specimen of urine (3.300 c.c.): urea, 1 per cent. or 33 grammes; albumin, 0.275 per cent.

20th. Examination of twenty-four hours' specimen of urine (2950 c.c.): specific gravity, 1006; urea, 32.45 grammes; albumin, 0.3 per cent.

Examination of Eye-grounds by Dr. Harlan. No new hemorrhages in right eye, and some of the old ones have been absorbed. Typical stellate appearance of macula. Large white patches of degeneration. In left eye there are a very few fresh hemorrhages, a number of large white patches, and decided changes in macula, which has typical splashed appearance.

August 6th. Operation by Dr. Gibbon. Left kidney was very large and very adherent to its fatty capsule, which was separated from it with difficulty. It was impossible to withdraw this kidney through the wound. Each pole, however, could be drawn into view, and with little difficulty the capsule was removed on both sides nearly as far as the pelvis. This kidney was not only large, but mottled and quite friable. The right kidney was not so large, but presented the same appearance. The fatty capsule here was also quite adherent, but the kidney was freed and withdrawn without much difficuly, and its capsule entirely removed and left rolled up near the pelvis. There was considerable oozing from the kidney surface, so that an iodoform drain was necessary. The time required for the opera-

tion on the left kidney, not including the closure of the wound, was fifteen minutes; that on the right, thirteen minutes. The entire operation, including the application of the dressing, was fifty-five minutes. Ether anæsthesia.

7th. Has had considerable pain, mostly in abdomen. Severe pain in back on slightest exertion. Wound is draining freely, some odor of urine.

8th. Urine: cloudy, pale yellow, acid, 1010, albumin, large quantity, no sugar, leucocytes, large amount of phosphates, and pale, granular, and waxy casts. Sleeps a great deal and wakens with a cry of pain. Bowels are very difficult to move.

12th. Passing good quantity of urine—sixty-seven ounces. Still growing more sleepy. Agonizing pain on motion. Given small amount of chloroform, and packing removed by Dr. Gibbon; fresh packing reinserted. Had some blood in bowel movements. Still urinary smell to bowel movements, and in the discharges from the wounds. Urine (total quantity examined, 770 c.c.): albumin, 3.465 grammes (Esbach method).

14th. During night pulse became full. Apex-beat very forcible. Had some twitching of face. Typically uræmic this morning. Breath is urinous, tongue dry and coated. Respirations full, deep, and noisy. Bled about twenty-two ounces and later given hot-pack, after which he perspired freely, but without improved condition. Urine (twenty-four hours' specimen, 740 c.c.): cloudy, dirty amber, white flocculent sediment, no sugar, amorphous urates, and excess of leucocytes, red blood corpuscles, epithelium, few hyaline and pale granular casts. Urea, 1.3 per cent. or 9.62 grammes; albumin, 0.8 per cent. or 5.92 grammes. Unconscious. Died 10.15 P. M. The temperature in this case was practically normal throughout the entire illness, with the exception that on August 6th, after the operation, it rose gradually, reaching 101° on August 8th and then gradually declining, being 99° on August 14th. As death occurred it again rose to 101.8° F.

Post-mortem (a complete one not allowed). Wounds were opened after death, and the following noted: The kidneys together weigh 320 gm. and measure 11 x 6 x 3 cm. Both are exactly similar. Except that on their removal from the body the capsule of the left was found to have been two-thirds stripped, while that of the right is only stripped over an area of 3 cm. on its posterior edge. On further stripping this kidney the capsule is found to strip with difficulty, leaving an extremely pale, yellowish-white surface. The stellate veins are very little marked, thereby contrasting with the portion which was already stripped, where they are quite prominent.

On Section. The kidneys are of a pale, yellowish-white color. The cortex averages 4 mm. in thickness, the glomeruli appearing as white spots. The striæ of the cortex are not visible. It has rather a granular, flaked look. The pelvis contains a fair amount of fat. Calices apparently normal.

The case just reported was one which in every respect seemed suitable for the operation recently devised by Edebohls for the cure of Bright's disease. The patient was young, still strong, and the expectation of life was some six months or a year, as far as could be judged. The

operation, however, failed to be of use and unquestionably hastened death, the result of pain, exhaustion, and disturbance of the kidney.

The pain was very great after the operation. In fact, I have never seen anyone suffer as much as this patient did.

Following the operation there was a marked falling off in the amount of urine as well as in the amount of urea secreted. Edebohls claims that improvement cannot be looked for until at least ten days after operation—the patient in this instance lived but eight.

The reason for failure of the operation to give benefit in this case may possibly be found in the contradictory statements contained in Dr. Gibbon's notes and in those at the post-mortem. Dr. Gibbon stripped the capsule back in both kidneys as far as the pelvis and left them inverted in the manner prescribed by Edebohls, expecting that they would contract and shrivel up. On the post-mortem table, however, but a comparatively small area of kidney surface was denuded in both kidneys, and the capsule was found adherent where Dr. Gibbon had stripped it away. There was no statement in the post-mortem notes whether or not any new vessels had formed and passed between the surrounding tissue and the kidney.

It is, of course, out of the question to draw conclusions of much value from a single case, and the report is read with a hope of eliciting some discussion as to the class of kidney disease best suited for this operation, and as to the technique of the operation itself. I was much impressed with the gravity of the operation, even in such a favorable case as this, in which the suffering was tremendous, and the result a rapid death from uræmia.

ORTHOSTATIC ALBUMINURIA. REPORT OF A CASE.[1]

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The etiology and clinical significance of functional albuminurias are not well understood. Within the last year or two several French physicians have offered a rational explanation for at least one variety, the so-called "albuminurie orthostatique," of which the following case is an example:

C. W., male, aged twenty-five years, single, cigarmaker, a native of Pennsylvania, complained of severe nervous symptoms and great weakness.

[1] Reported at a meeting of the Clinical Section of the Medical and Chirurgical Faculty of Maryland, December 12, 1902.

Family History. Father died of apoplexy at the age of sixty-six years; the mother is living, aged sixty-two years, she suffers from indigestion; six brothers and five sisters are living and in good health.

Past History. Had measles, whooping-cough, and mumps as a child; at the age of thirteen years a severe attack of diphtheria; for the past four or five years the patient has been suffering from nervous dyspepsia.

His occupation confined him within doors, his working hours were long; for several years has enjoyed very little outdoor life. Alcohol and tobacco are taken very moderately. There is no history of specific infection.

For the past three years the patient has been a sexual neurasthenic and has complained of many of the subjective symptoms characterizing general neurasthenia, such as extreme irritability, weakness, mental depression, fear of sickness, vertigo, sleeplessness, palpitation of the heart, and vague sensory and vasomotor disturbances.

About one year ago he was examined for life insurance and albumin was found in his urine. He was treated for seven months for this condition and his nervous symptoms without any apparent improvement.

When I first saw the patient, on May 15, 1902, his general condition was fairly good; he was rather poorly nourished and weighed one hundred and thirty-seven pounds. The skin was sallow; there was a slight pallor of the lips and conjunctiva; the face was either flushed or pale, and the expression nervous.

Chest. Well developed; respiratory rhythm and sound normal.

Heart. Position of apex normal. No forcible impulse at apex; no increase in area of cardiac dulness; no accentuation of second aortic sound; no murmurs.

Pulse (sitting), 82; rhythm good; tension and volume normal.

Liver and spleen negative. Kidneys not palpable.

Digestive System. Tongue slightly coated; appetite good; but for some time there has been a sense of pressure over the epigastrium which is most marked half an hour after eating, and is associated with nausea, eructations, and a feeling of general weakness.

Physical examination of the stomach negative. (No test meal was made at this visit.) His bowels were inclined to be constipated.

Nervous System. Sensorium rather dull; suffered very little from headache, but had occasional attacks of vertigo; sleep, restless; did not feel refreshed in the morning. No marked tremors.

Had a general hyperæsthesia and a paræsthesia confined to the lower abdomen and both legs; these sensations were generally tingling in character. He also had girdle-like pains occurring three or four times a day, and lasting from half to one hour.

The tendon reflexes were slightly diminished; skin reflexes normal.

Vasomotor symptoms were quite marked. Morbid flushing of the face alternated with extreme pallor. The hands were purple and congested and the feet felt as if they were swollen, except when lying down. Factitious urticaria was particularly well marked, especially over the chest and abdomen. The superficial veins of the extremities were very prominent and felt tense.

Red blood count 4,400,000. No leucocytosis.

Urine. Patient voided urine frequently, which was sometimes accompanied with a slight burning sensation. He rarely passed less than four pints in twenty-four hours.

The first specimen examined was voided in the evening, after supper, and after he had been walking and standing a great deal during the day. It had a specific gravity of 1030, and contained 0.7 per cent. serum-albumin (Purdy's method), a few hyaline casts, squamous epithelium, and pus cells.

The patient was instructed to bring two specimens the next day, one of the morning's urine upon rising and another of the urine after moderate exercise. An examination showed that the morning's urine was entirely free from albumin, and that voided at noon contained a considerable quantity. At 3 P.M. I examined a specimen of freshly voided urine; he had been on his feet for several hours, but had done very little walking; it was found to contain 0.1 per cent. The patient remained seated in my office from 3 to 5 P.M., when another freshly voided specimen was examined. This time the reaction was absolutely negative for serum-albumin.

Similar observations were made on the following day which showed practically the same result, as follows: Morning urine negative. Urine passed at 12.30 P.M., after walking, marked traces of albumin. Urine passed at 5 P.M., after walking, marked traces of albumin. Urine passed at 8 P.M., after standing, 0.3 per cent. of albumin. Microscopically, most of these specimens contained hyaline casts; they were otherwise negative.

The treatment prescribed was outdoor life, with moderate exercise, restricted proteid diet, cold wet-packs at night, and tincture nux vomica and syrup hypophosphites (U. S. P.) before meals.

On June 18th, one month later, the patient again reported, when the following notes were recorded:

"General condition is decidedly improved; there has been a gain of two and one-half pounds in weight; he appears to be less nervous; the appetite is improved, there is less nausea; the bowels are still constipated; he sleeps better and feels more refreshed on waking in the morning. He has been able to take more exercise and has felt less fatigued afterward."

He brought two specimens of urine voided May 20th; one, passed after standing quietly for two hours, contained 0.1 per cent. albumin; the other, passed two hours later after resting in a chair, was absolutely free from albumin.

June 16th. Five specimens were examined: (*a*) Morning urine negative. (*b*) Urine passed at noon after playing baseball, slight traces of albumin. (*c*) Urine passed at 2.30 P.M. after dinner and moderate exercise, marked traces of albumin. (*d*) Urine passed at 6 P.M. after a period of rest (sitting), negative. (*e*) Urine passed at 9.30 P.M. after exercise, contained traces of albumin.

17th. Two specimens: (*a*) Urine passed at noon after dinner and considerable exercise, had marked traces of albumin. (*b*) Urine passed before supper and after no exercise, negative.

Hyaline casts were found in only a few of the specimens.

Alternate hot and cold spinal douches in the morning were added to the previous treatment.

July 15th, his next visit, the patient had gained four pounds in weight; he endured exercise with much less fatigue, but complained of having, at times, a feeling of general depression, lasting from two to three hours, and was annoyed with distress in his epigastrium in the

morning after eating breakfast. His appetite had remained good and bowels had been regular.

A test meal was made and 85 c.c. of gastric contents removed, which gave a total acidity of 80, and contained a large amount of clear, stringy mucus. He was directed, in addition to previous treatment, to wash out his stomach every morning before breakfast.

7*th.* Four specimens of urine examined for albumin were negative.

8*th.* Of four specimens examined three were negative; the other specimen, voided before going to bed and after a long period of standing, contained traces.

15*th.* Two specimens examined were both negative. No casts were present in any of these specimens.

The patient again reported on August 12th, much improved. He felt relieved of most of his nervous symptoms and he had a better color and expression. His weight was the same as at the last visit. The distress after eating had been considerably relieved by lavage.

A test meal was made and 140 c.c. of gastric contents were removed. The total acidity was 85.

Of six specimens of urine examined, one contained 0.25 per cent. albumin. This specimen was voided at 10 P.M., after the patient had been on his feet for several hours, standing most of the time. The ice-packs, spinal douches, and lavage were continued. Tincture nux vomica was ordered in increasing doses before meals, and a powder was prescribed, containing prepared chalk, calcined magnesia, and bicarbonate of soda, to be taken after meals.

September 22*d*, the patient felt very well; he had gained four pounds in weight and was entirely relieved of his gastric symptoms; one specimen of urine examined was negative.

November 17*th*, his last visit, the following notes were taken: "General appearance good; there is a tendency to flushing of the face and spurious urticaria is present; weight one hundred and forty-eight and a half pounds—a gain of eleven and a half pounds since the first visit; the appetite is very good, he eats the ordinary mixed diet and has no distress after eating; the bowels are regular; sleep is undisturbed; micturition is normal and about 2000 c.c. are passed daily; the urine is negative for albumin; five specimens of urine were examined."

The lavage and powders of chalk, magnesia, and soda were discontinued the latter part of October, the gastric symptoms having been entirely relieved.

The wet-packs were continued regularly for three months and occasionally after that time. Tincture nux vomica was taken throughout the entire course of treatment.

The patient resumed his former occupation about November 1, 1902, and, thus far, has experienced no ill effects.

SUMMARY. Of 36 specimens of urine examined, extending over a period of six months, the specific gravity averaged 1026.2; the percentage of urea 2.45 per cent. Serum albumin was present in 12 specimens, 10 of which occurred in the first 16 specimens examined, covering the first month of treatment. The other 2 in the last 16, covering five months of treatment. Of 8 specimens examined before treatment the specific gravity averaged 1028.3 against 1025.8 after treatment, and the

percentage of urea 2.8+ per cent. against 2.3 per cent. after treatment.

If we recount the striking facts in this case—serum albumin appearing in the urine when the patient is in the upright posture, standing; diminished by exercise or fatigue, not influenced by diet; disappearing in the sitting or horizontal position; the high specific gravity; the normal or moderately increased percentage of urea; no casts except hyaline; no organic changes in the cardiovascular system; but a marked disturbance of the vasomotor system, we have the very interesting symptom-complex which has recently been described by several French writers as orthostatic albuminuria.

I wish to refer especially to Dr. J. Vire's valuable contribution in the form of a thesis, extracts of which have been published.[1] According to this author, orthostatic albuminuria is a form of albuminuria in which the station is the only factor producing the condition. It appears only in young persons who are otherwise apparently healthy. It is not influenced by fatigue, habit, or milk diet, and is not accompanied by any of the functional conditions associated with Bright's disease.

The discovery is purely accidental and depends upon methodical examination of the urine. Standing immobile will cause albumin to appear; it disappears on assuming the horizontal position. Albumin may persist while the patient is walking, but walking alone does not suffice to produce albuminuria. No functional condition in other organs can explain this form of albuminuria. There are, in all cases, certain vasomotor disturbances, such as cyanosis of extremities, or hay fever; this suggests a nervous origin of this phenomenon.

The examination of the urine reveals a fluctuating character and is associated with symptoms of catarrh of the urinary passages and the presence of nucleo-albumin and mucus. The quantity, color, and density are about normal. The urine is rich in salts, such as urates, phosphates, and oxalates. The quantity of serum-albumin does not exceed one gramme in twenty-four hours. The serum-albumin points to the renal origin of the process.

Diagnosis. A positive diagnosis is simple. The differential diagnosis must be made from the albuminurias of Bright's disease; of cardiac and digestive origin, of tuberculosis, of Pavy's disease, and finally from the albuminuria of fatigue. Cases may occur in which these forms are combined.

The prognosis is benign; cases are often cured spontaneously when there is a gain in the individual's weight.

None of the cases observed by Vire resulted in Bright's disease.

Orthostatic albuminuria occurs equally in both sexes. It occurs in neuropathic and slightly anæmic adolescents presenting a nervous or

[1] L'Independence Médicale, 1901, No. 19.

diathetic heredity, and is always associated with an appreciable disturbance of the vasomotor system.

Orthostatic albuminuria seems to be due to fluctuating congestion of the kidney, a vasomotor disturbance of the renal circulation. It may be compared to the cyanosis of the extremities which is produced by the same cause.

Aubertin and Rogers[1] reported five cases of distinctly orthostatic albuminuria following scarlet fever. Aubertin believed it to be the terminal stage of a previous nephritis and a disturbance in the circulation of the kidney.

Rudolph[2] believes that this form of albuminuria is the result of venous stagnation. The fact that the upright posture causes the albuminuria indicates that it is physical. He thinks that it is the result of previous inflammation of the kidneys and lack of elasticity of the vessel walls in the glomeruli.

Niviere[3] reported a case of orthostatic albuminuria in a young man, aged twenty years, who had dyspepsia for five years, and had had scarlet fever at the age of seven years. The patient had a movable right kidney. There was one gramme of albumin to the litre of urine. A flannel binder relieved the condition, but the albumin reappeared when the binder was removed. Niviere believes that the albuminuria was due to mechanical causes, which disappeared when the abdominal viscera were kept in place.

The treatment, as directed by Vire, is hygienic, strengthening, and antinervous, the line adopted in this case in which the albuminuria disappeared in one month.

ON THE OCCURRENCE OF EHRLICH'S DIMETHYLAMIDOBENZALDEHYDE REACTION IN THE URINE.

By Charles E. Simon, M.D.,
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About two years ago Ehrlich[4] pointed out that under certain conditions dimethylamidobenzaldehyde produces a red color with certain mucins, and that a similar reaction may be obtained with both normal and pathological urines. He was guided in his experiments by a knowledge of the readiness with which the aldehydes react with various chemical substances, and notably with anilins and phenols. By making use of aldehydes which furnish colored compounds, his view was, if

[1] La Presse Médicale, October 9, 1901, No. 81.
[2] Centralblatt f. innere Medicin, February 24, 1900, 21 Jahrg., No. 8.
[3] Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris, 1901, No. 6.
[4] Ueber die Dimethylamidobenzaldehydreaction. Med. Woch., 1901, No. 15.

possible, to demonstrate still unknown constituents belonging to this class. He found that in various pathological urines, notably in phthisis, typhoid fever, and chronic enteritis, a fine, cherry-red color develops on shaking the urine with a few drops of the reagent in acid solution, and that the resulting pigment can be in part extracted with chloroform, and almost entirely so with epichlorhydrin or dichlorhydrin. It was further ascertained that normal urines also give the reaction, but that this is much less intense, and if done at ordinary temperatures a distinct red color does not develop. On heating, however, it becomes apparent and can likewise be demonstrated by extracting with epichlorhydrin. But even then the intensity of the reaction is not at all comparable to what is seen in disease. Ehrlich suggested at the time that it would be of interest to study the reaction in question in a large number of cases, and to ascertain the conditions under which the intensified reaction occurs. I began my observations after seeing Ehrlich's paper and have continued them, with unavoidable interruptions, ever since. As the urinary material which has been at my disposal, however, has not been very large, my investigations could not be so extensive as I should have liked. My single examinations, however, are, nevertheless, sufficiently numerous to warrant their report at this time, and I have been further impelled to publication by the fact that two papers on the same subject have already appeared in the foreign journals.

The first clinical report was made by Clemens.[1] His results in summary are the following: The intensified reaction, with which alone we have to deal in the present paper, was never observed in health. It was most commonly seen in acute gastrointestinal affections, and among these practically only in the inflammatory forms or those depending upon tumors. Pure cases of gastritis and enteritis individually very curiously did not give the reaction. In the common gastroenteritis of the summer months it was found in three-fourths of all cases. In chronic enteritis it was relatively less common, but was occasionally found, once quite intensely in an alcoholic patient. Of nine cases of appendicitis, six gave positive results, and it was observed that in some it persisted even after the disappearance of the clinical symptoms. It was positive in some cases of simple constipation and in one case of lead colic. Of three cases of carcinoma of the stomach it was absent in one, occasionally present in the second, and apparently constantly present in the third. In one case of carcinoma of the œsophagus also it was always found.

Negative results were obtained in dilatation and ulcer of the stomach,

[1] Zur Ehrlich'schen Dimethylamidobenzaldehydreaction. Deutsch. Arch., 1901, vol. lxxi. p. 168.

in enteroptosis, non-tuberculous peritonitis, hepatic cirrhosis, intestinal tuberculosis, and acute intestinal occlusion.

Of diseases of the respiratory organs, three cases of pneumonia of five gave the reaction, as also one case of acute febrile bronchitis, while the great number of the acute and chronic bronchitis cases and two of bronchial asthma gave negative results.

Of eight cases of pleurisy the reaction was obtained in two and it is noteworthy that both individuals were tuberculous.

Two cases of empyema, of which one was complicated with miliary tuberculosis, did not react, but in a case of subphrenic abscess the reaction was constantly present.

Of twenty-six cases of pulmonary tuberculosis, nine gave a positive result, and it is noteworthy that not all of these were complicated by gastrointestinal disturbances. In this connection Clemens introduces a summary of the results which were obtained in pulmonary tuberculosis at a certain sanatorium, by Dr. Engel, which I reproduce:

"The reaction is positive in connection with acute gastrointestinal —notably, intestinal—disturbances. It is frequently positive, with a simultaneously positive diazo reaction. Tuberculosis *per se*, even the febrile advanced form, does not necessarily call forth a positive reaction. Frequently it was present on admission and disappeared within a few days after the arrival of the patient. In cases in which a positive reaction was obtained the urine was constantly of high specific gravity —1028 to 1032. With its disappearance the specific gravity also fell to normal. It is noteworthy, however, that by artificially concentrating the urine a positive result could not be produced in the negative cases."

Clemens then continues his personal observations: A positive result was obtained in one case of tuberculous meningitis, in one of tuberculous pleurisy and peritonitis, and in one of miliary tuberculosis.

Acute diseases of the endocardium and pericardium, as well as valvular lesions in the absence of complications, and further cases of nephritis and cystitis, gave negative results. In one case of pyelocystitis, however, the reaction was present.

Negative results were obtained in the diphtheritic and non-diphtheritic anginas, in cases of acute articular rheumatism, and also in two cases of scarlatina, while of six cases of measles two reacted positively. Of six cases of facial erysipelas three gave a positive reaction, which persisted in one at least with great intensity into convalescence. Only three cases of typhoid fever were examined, and of these only one gave a positive reaction, which was pronounced and persisted for some time.

In several cases of diabetes and glycosuria a negative result was obtained. A case of morbus maculosus Werlhofii, with fairly severe

symptoms at first, gave a positive reaction continuously, which later disappeared.

In two cases of brain tumor the reaction was negative.

Important is the observation of Clemens that all stools which he examined, both normal and abnormal, gave a distinct bluish reaction of approximately the same intensity in all, and the same was observed in the case of the distillate. As pure indol also gives the reaction it is quite likely that the fecal reaction is referable to this source. Whether it is identical with the urinary reaction remains to be seen. Urines which are rich in indican do not necessarily give it, as we shall see.

The second clinical report is made by Koziczkowsky[1] and comes from Senator's clinic. His results follow:

A constant reaction, viz., present from the first observation until death, was observed in five cases of pulmonary tuberculosis, one of pulmonary tuberculosis associated with tuberculous peritonitis, and in one case of fibrinous pneumonia. All six cases of tuberculosis presented a very severe form of the disease and were associated with rapid wasting; especially high temperatures were not observed. In connection with this first group he further mentions two cases which had not gone on to a fatal end yet at the time of the report, but in which the reaction was also constantly present. The one was a case of infectious cholecystitis and cholangitis, in which the urine contained bile pigment; on some days on which the urine contained specially large amounts of bilirubin the red color was not seen, but in its place a dark, dirty, greenish shade. The second case was a severe endocarditis, with very high and subnormal temperatures, following acute articular rheumatism. Both cases were rather hopeless.

In his second group Koziczkowsky has collected five cases in which the reaction was not continuously, but only temporarily, present. It comprises one case each of fibrinous pneumonia, of pulmonary tuberculosis, of acute endocarditis, acute articular rheumatism, and of scarlatina. In these five cases the reaction was constantly present for some time, and it was noted that with an improvement of the subjective and objective symptoms there was at first a diminution in the intensity of the reaction, which then gradually disappeared. He adds three cases to this group in which a negative result was obtained for some time following admission, but in which it gradually appeared. One of these cases was a chronic bronchitis with bronchiectasis, the second a pulmonary tuberculosis, and the third a pulmonary tuberculosis associated with nephritis. In all three the appearance of the reaction was associated with a deterioration in the patient's condition.

In all other cases which were examined negative results were

[1] Berl. med. Woch., 1902, vol. xxxix., No. 44.

obtained. These comprise seven cases of pulmonary tuberculosis, one of pneumonia, seven of chronic nephritis, two of splenic anæmia, three of subacute articular rheumatism, four each of acute diarrhœa, chronic enteritis, neurasthenia and constipation, and one each of gonorrhœal arthritis, erysipelas, acute articular rheumatism, angina, endocarditis, chronic bronchitis, diabetes mellitus, traumatic neurosis, influenza, hepatic cirrhosis, carcinoma of the liver, carcinoma of the stomach, achylia gastrica, angina pectoris, tabes, Landry's paralysis,and tertiary syphilis.

In attempting to ascertain the relationship between the occurrence of the reaction and the degree of intestinal putrefaction, Koziczkowsky also made parallel indican examinations in his cases, but was unable to establish any definite relation.

Experiments on rabbits which were further undertaken to ascertain the influence of increased tissue destruction upon the reaction likewise yielded no results. Of special interest also is the observation that Koziczkowsky was unable to obtain the reaction in the œdematous fluid of a patient in whose urine the reaction was constantly present with great intensity.

In my personal examinations I employed a 2 per cent. solution of dimethylparamidobenzaldehyde in equal parts of water and concentrated hydrochloric acid. A few cubic centimetres of urine in a test-tube are treated with from five to ten drops of the reagent; the mixture is set aside or agitated for a few minutes and the color then noted. Normal urines usually turn a greenish-yellow, or the normal color merely becomes intensified. At times a dark amber color develops, though this is less common in health, unless the urine is brought to the boil before the reagent is added. In this way it is a common experience to meet with moderately or dark amber tints. With these reactions, however, I have not occupied myself, and, like Clemens and Koziczkowsky, I have only noted the reaction as positive when a distinct *cherry-red* color developed, either immediately on adding the reagent or after agitation or standing. This reaction I have never noted in health, though many urines from supposedly normal individuals were examined. That the substance which gives the pathological reaction is present, however, can often be demonstrated even then by extracting with a little chloroform or, still better, with epichlorhydrin, which will take on a more or less well-marked pink color. In my observations in disease, heat was not applied. In every case the urine should be as fresh as possible; certainly not older than twelve hours, for I have often noticed that a urine which gave an intense red on the afternoon of one day scarcely reacted at all on the next morning or merely gave a dark amber color. Most likely the substance which gives the reaction is readily decomposed and all attempts at preservation which I have made have thus far proven futile.

In this connection it is important to note that the presence of formalin will prevent the occurrence of the reaction, as has been demonstrated by Ehrlich, Pröscher, and Nicolaier, independently of each other, and as can be readily demonstrated as follows: Of a urine which gives a well-marked reaction a few cubic centimetres are placed in two test-tubes. To the one specimen a few drops of formalin solution are added and then the reagent to both. The formalin specimen retains its previous normal color, while in the other the red develops. In this manner a convenient control-test can be made in doubtful cases. The negative reaction in the case of the formalin specimen is explained by the fact that the formalin has probably united with the group of the urinary body, which would otherwise have combined with the benzaldehyde.

The intensity of the red color in disease, as I have stated before, is variable. Sometimes it develops almost immediately when the first drop of the reagent falls into the urine; at other times it is necessary to wait for from two to four minutes before the full intensity is reached. To wait much longer than five minutes is not always safe, as the red color disappears again on standing and is replaced by the more common dark amber. However, I have also seen the red color persist for several days, but only in the case of urines which gave a very intense reaction.

As regards my positive results, I may state at once that there was no single disease in which the reaction was obtained in every case, and that even in one and the same individual the reaction was not constantly present. Positive findings were noted in pulmonary tuberculosis, tuberculosis of the hip-joint, pneumonia, typhoid fever, appendicitis, embarras gastrique, icterus, malignant endocarditis, traumatic neurosis, empyema, and œsophageal carcinoma. My list of negative cases, on the other hand, includes first of all a large number of normal or supposedly normal individuals, further cases of normal labor, neurasthenia, hysteria, diabetes, aortic aneurism, myelogenous leukæmia, lymphatic leukæmia, acute nephritis (scarlatinal), simple diarrhœa, morphinism, valvular disease, phthisis (stationary), diphtheria (before and after the use of antitoxin), typhoid fever, cases of abortion, appendicitis, influenza, chronic nephritis, cystitis, pyelitis (calculous), measles, tuberculosis of the hip-joint, cystic kidney, carcinoma of the kidney, tonsillitis, acute and chronic bronchitis, pneumonia, icterus, tubercular peritonitis, general erythema, varicocele, following various operations, such as nephrorrhaphy, removal of pus tubes, operation for vesico-vaginal fistula, fistula in ano, and suspension of the uterus. Examination of a urine containing cystin and diamins also was negative. A comparison of the negative with the positive cases will show at once that not all cases of pulmonary tuberculosis, tuberculous hip-joint dis-

ease, pneumonia, typhoid fever, appendicitis, and icterus give a positive result. So far as tuberculosis is concerned, however, it appears that the reaction is more likely to occur in the actively progressive cases than in those which are more or less stationary. It was also noted that the positive cases almost all gave a positive diazo reaction, while in the negative cases this was not obtained. Exceptions, however, are encountered, and it may be stated at once that the occurrence of the benzaldehyde reaction is not at all dependent upon the diazo reaction. This is seen very well in the typhoid cases, where the diazo reaction is so very common and constant, while the benzaldehyde reaction is a most variable factor. In one of my typhoid cases, in which a marked diazo reaction was noted throughout the greater part of the disease, the benzaldehyde reaction was constantly negative.

In the study of the typhoid cases an interesting observation was incidentally made. It was noted that in one instance in which a positive diazo reaction was kept up artificially by the administration of naphthalene, the benzaldehyde reaction was not obtained. This is of moment in the determination of the character of the combining substance.

Noteworthy is the frequency with which the reaction is seen in pneumonia, but it is manifest that its presence here is not an index of the severity of the condition. For, on the one hand, I have obtained a most intense reaction in severe cases that ended in recovery, while, on the other hand, it may be but little pronounced late in the course of fatal cases. In one instance with delayed resolution the reaction was faint on the twelfth day of the disease, distinct on the thirteenth, death occurring on the fourteenth.

In a case of empyema the reaction was quite marked before the operation, so also on the day after operation, while later it was negative.

That elevation of temperature *per se* has nothing to do with the appearance of the reaction is well shown by the typhoid cases, and is further manifest from a study of the febrile diseases, such as acute bronchitis, influenza, tonsillitis, measles, etc., in which negative results only were obtained. Cyanosis also, *per se*, is not the causative factor, as the reaction was present in conditions in which no cyanosis occurred, on the one hand, and absent in others in which there was marked lack of oxygenation.

As a matter of fact, it is difficult to point out one single factor which is constantly present and common to all the positive cases. My impression, however, is that the reaction is most likely to occur in conditions in which there is marked and rapid destruction of tissue albumins. This is suggested especially by the case of traumatic neurosis in which a positive reaction was obtained. The patient in question received an

injury to the head, and was thereafter reported to have been unconscious for two or three weeks. Three months later, when he was first seen by Dr. Beach, of Baltimore, to whom I am indebted for these notes, he was much emaciated and made the impression of a person in the last stages of consumption. His pulse then was 48 and the temperature 97° F. There was no cough, no sputum, and physical examination showed the lungs to be clear. The total loss of flesh was between 60 and 75 pounds. There was no diazo reaction, but the benzaldehyde test gave a positive result on every occasion. Subsequently the patient entered suit for damages and was awarded a sum of money. Since then his health has been much improved; he has now gained about thirty pounds and the benzaldehyde reaction is absent.

As I have said, this case in its bearings on the causation of the reaction seems quite suggestive. The patient at the time of the accident was a healthy, robust man without evidence of any organic lesion; at no time was there any fever, gastrointestinal disturbances, or cyanosis. The one controlling factor of the case was the rapid and progressive loss of flesh; while this was actively going on and when the patient was already much emaciated, the reaction was present; later, when the nutrition of the man had improved, it was absent.

The one case of icterus in which the reaction was positive, corresponded in a general way with the complex of symptoms described by Weyl. Bearing in mind that certain constituents of the bile give a color reaction with Ehrlich's sulphanilic acid test, it appeared of interest to test the bile directly with the benzaldehyde also. The material for the test was obtained from a biliary fistula, which had remained after an operation for gallstones; the result was entirely negative.

Quite recently finally I had occasion to again examine the urine of one of the cystin cases which I have previously reported[1] and in which cadaverin was constantly present; in this case, also, negative results were obtained.

If, then, I summarize my clinical results, we may conclude:

1. That the benzaldehyde reaction does not occur under normal conditions, meaning, of course, the pathological grade of the reaction, viz., the direct occurrence of a red color.

2. Positive reactions are most commonly obtained in cases of tuberculosis.

3. The reaction is also seen in non-tuberculous cases, both febrile and non-febrile.

4. It is not dependent upon the presence of the body which gives rise to the diazo reaction.

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1900, vol. cxix. p. 39.

5. For its production elevation of temperature, gastrointestinal disturbances, and cyanosis are not essential.

6. Common to all cases seems to be an increased catabolism of the tissue albumins. This final conclusion, in my opinion, is not rendered negative by Koziczkowsky's experiments on rabbits, and merits further investigation.

As regards the chemical reaction which takes place on the addition of the reagent to the urine, it is likely that the aldehyde group reacts with a methylene or amido group of a still unknown constituent, in the sense of the following equation, in which x represents a radicle of this order:

$$C_6H_4\begin{matrix}N(CH_3)_2\\CHO\end{matrix} + H_2X = C_6H_4\begin{matrix}N(CH_3)_2\\CH=X\end{matrix} + H_2O.$$

Of the known constitutents of the urine none gives the reaction As I have pointed out, Clemens has ascertained that the feces of normal as well as of diseased individuals always gives a positive reaction, and that this is in all likelihood due to the presence of indol, which itself gives the reaction. In the case of the urine this observation cannot enter into consideration, as the indol does not appear here in the free state, but as indican, and to a less extent as indoxyl glycuronic acid. A relation between the elimination of indoxyl and the reaction in question, however, does not exist. This has been shown by Clemens and Koziczkowsky, and I have also arrived at the same result. The reaction is sometimes observed coincidently with a pronounced indican reaction, but at other times it may occur even though no indican is demonstrable by the usual tests. One individual that I have been able to observe for years, and who always shows an intense indican reaction, has never given the other, although I have frequently examined in this direction.

All attempts at isolation of the urinary constituent in question have thus far not led to satisfactory results. This is due primarily to the fact that the body is manifestly quite unstable, and that after the disappearance of the reaction from a urine which gave it a short while before it cannot be made to reappear. Momentary ebullition is apparently without effect, but on evaporating the urine the reaction promptly disappears. Appropriate extractives or precipitants are also unknown. Pröscher[1] states that after saturating the urine with ammonium sulphate the body can be extracted in part with amyl alcohol; but as it is present at best only in traces, this method is altogether inapplicable for the purpose of isolating larger amounts.

The red pigment, on the other hand, can be successfully isolated, as

[1] Zur Kenntniss d. Ehrlich'schen Dimethylamidobenzaldehydreaction. Zeitsch. . physiol. Chem., 1901, vol. xxxi. p. 520.

has been shown by Pröscher, who obtained the following analytical results: carbon, 56.49 per cent.; hydrogen, 7.06 per cent., and nitrogen, 8.28 per cent.; a molecular determination gave 275, from which the formula $C_{16}H_{24}O_6N_2$ resulted. This represents the compound of the aldehyde and the urinary constituent. By deducting from this the group $C_9H_{11}N$, viz., dimethylamidobenzaldehyde, —O, and adding two atoms of hydrogen, we obtain the formula $C_7H_{15}O_6N$ for the unknown body. This formula only differs by the group COH_2 from that of glucosamin—$C_6H_{13}O_5N$—and we could, accordingly, imagine that it represents a formyl-glucosamin or the acetyl derivative of the still unknown pentosamin.

Clemens examined a glucosamin prepared according to Ledderhose, as also a glucosamin, a fructosamin, and a lactosamin, after Lobry de Bruyn, in reference to the reaction, but obtained negative results.

Of special interest in this connection are certain observations which Müller[1] incidentally made in this direction. He cites Ehrlich as authority for the statement that chitin, pure chitosan, glucosamin hydrochlorate, and mucin in itself do not give the reaction; but that it may be obtained with mucin after careful treatment with caustic alkali. Müller was able to confirm Ehrlich's observations in the case of pure mucin obtained from sputum, and also obtained positive results after treating with caustic alkali and heating gently, in the case of submaxillary mucin, ovomucoid, the pseudomucin from ovarian cysts, egg albumen, as also with mucoid sputa and cartilage. He further ascertained that Weydemann's animal gum, which is still quite closely related to its mother-substance, submaxillary mucin, also gave the reaction after boiling with caustic alkali, but not directly. Fränkel's albumin, on the other hand, which may be regarded as the hydrolytic product standing next in order after Weydemann's animal gum, gave the reaction at once. This albumin, according to Fränkel, is a polymeric compound of glucosamin, and it is the more remarkable that it gives the reaction, since Hoppe-Seyler's chitosan, which is likewise a polymer of glucosamin, does not do so, according to Ehrlich.

In order to ascertain whether glucosamin hydrochlorate does not give the reaction because the amido group is bound by the hydrochloric acid, Müller heated the aqueous solution of the hydrochlorate with potassium hydrate or baryta-water, and then added sodium acetate in order to prevent the appearance of free hydrochloric acid. The aldehyde was then added and an amount of acetic acid sufficient to render the fluid strongly acid. It was found, however, that the presence of a mineral acid is essential to the production of the red color, and that glucosamin in acetic acid solution does not give the reaction. Müller

[1] Beitr. z. Kenntniss d. Mucins und einiger damit verwandter Eiweisstoffe. Zeit. f. Biol., 1901, vol. xlii. p. 561.

further studied the question in the case of pentabenzoyl glucosamin, but likewise only obtained negative results, even after heating with caustic alkali, whereby several benzoyl groups are split off. An aqueous solution of penta-acetyl glucosamin likewise did not react as such, but in this case an intense reaction was obtained on the application of mild heat, if the test were made after the substance had been previously heated with sodium hydrate or baryta-water. This step, however, cannot well have resulted in any other change than the splitting off of one or more of the acetyl groups and the resultant formation of a monoacetylglucosamin or diacetylglucosamin. From this observation the conclusion naturally suggests itself that the red color only develops on treating with dimethylamidobenzaldehyde, if the glucosamin is still united with one or more acetyl groups.

SYPHILIS AS A CAUSE OF CHOREA.[1]

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Like most of the so-called functional neuroses, chorea is notorious for the multiplicity of its causes and remedies. One would expect this after a moment's consideration of the name and symptomatology of the disease. The effort to establish chorea as a "definite, substantive affection" (Osler), or as a "distinct malady, showing varying degrees of permanence and intensity" (Dana), is far from being entirely satisfactory. The enumeration of such diverse etiological influences as fright, peripheral reflex irritation, and infectious blood states toward the production of a definite, uniform affection is, to say the least, somewhat anomalous. Hence there is ground for the contention that under the name chorea many varied conditions have hitherto been discussed. This is particularly obvious after a careful comparison of the minor and major choreas, Huntingdon's and Friedreich's diseases, the hysterical and electric choreas, the various tics and symptomatic choreas. Between all these affections there is only an apparent similarity in regard to the muscular jactitations.

The term *chorea* literally means a dance, and, as applied to the irregular, inco-ordinated, jerking movements of the voluntary muscles, indicates a mere symptom rather than a disease. As a symptom it reveals a functional disturbance of the higher or volitional or inhibitory motor neurons, which disturbance, on account of its functional

[1] Read before the Chicago Medical Society, March 4, 1903.

character, may be the result of various irritative causes. The probability of this assertion rests upon many facts, chief of which is that there are no constant pathological findings.

Some authors make a distinction between symptomatic or organic chorea and ordinary chorea, meaning by the former the choreiform movements produced by gross organic lesions, and by the latter Sydenham's disease. Such distinctions, however, lead to confusion and contradiction. Dana, for instance, like most writers, distinguishes between symptomatic and ordinary chorea, and then for the latter assigns such pathological changes as "intense hyperæmia, with dilatation of vessels, small hemorrhages, and spots of softening," which, acting as "points of irritation in the cortex and its meninges and in the deeper parts, excites irregular discharges of nerve force and produces the choreic movements." If this is not symptomatic and organic as truly as the chorea due to any other form of gross lesion, I do not understand the meaning of the term symptomatic. As a matter of fact, all choreiform movements are symptomatic, and the differences in their character are due to the differences in the character and location of the irritative lesion. So far as being a symptomatic disease, acute minor chorea is as dependent upon a physical basis as any of the other forms of chorea. The nature of this physical basis may not be entirely clear, but that it is molecular, chemical, bacteriological, or even minutely organic can hardly be doubted.

Among the causes of acute minor chorea, the infections play a large rôle. The authorities enumerate rheumatism, pneumonia, scarlet fever, gonorrhœa, puerperal fever, typhoid fever, pyæmia, and septicæmia. That functional or organic changes of some sort are instituted by these various infections goes without saying, and argues for the symptomatic nature of even Sydenham's disease. Osler remarks that the "prominent psychical element is certainly one of the most serious objections" to the infectious theory of the origin of the disease, "since there can be no doubt that ordinary chorea may rapidly follow a fright or a sudden emotion."

The objection would be a valid one if chorea minor were a "definite, substantive affection" and not merely a symptomatic trouble.

Among the infectious causes of the choreiform phenomenon, syphilis is rarely mentioned, either in the books or in the current literature. Moreover, a search through the literature has rewarded me with the reports of but a small number of cases of syphilitic chorea. To this number I will add another case.

Under the title "Some Cases of Syphilitic Chorea," Robert H. Alison stated in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES for July, 1877, that "Chorea due to syphilitic disease of the nervous centres is so rare that up to this time, after an extended research, I

have been able to find only two cases recorded." Of these two cases, one was unilateral, the other generalized. To these two cases Alison contributed two more, both unilateral, from the private notes of Weir Mitchell and the records of the Infirmary. The case of generalized chorea was reported by Zambaco as Obs. 76 in his *Affections Nerveuses Syphilitiques*. It occurred in a seamstress, aged twenty years. The jactitations appeared after the syphilitic infection and before the appearance of the eruption. A cure was accomplished in five months. Anent these four cases, Alison remarked that spasm of the vessels and altered molecular states of nerve tissue would not explain them. There was doubtless, he says, a positive lesion, probably vascular occlusion of the minute vessels of the corpus striatum and neighborhood. This would seem more likely to be true of the unilateral cases than of the generalized one. Such cases bear to general chorea a relationship somewhat like what monoplegia bears to general functional paralysis, or what Jacksonian epilepsy bears to idiopathic epilepsy. It is difficult to imagine what sort of a "positive lesion," unless we include toxæmia and some of its immediate results in that category, could provoke a generalized chorea. This difficulty is still greater in connection with those choreas which seem to depend upon inherited syphilis. Syphilitic arteritis and meningitis are positive lesions of a generalized character, dependent primarily, however, upon a generalized cause—the toxic state of the blood.

Two cases of chorea associated with congenital syphilis are reported in the "London Letter" of the *Philadelphia Medical Times* of April 14, 1877. One of the cases was that of a boy, aged seven years, with hemichorea. The other, his sister, aged twelve years, was a case of bilateral chorea. Both cases exhibited unmistakable signs of inherited syphilis, and both were promptly cured of the choreiform attack by the use of antisyphilitic medication.

Rare as syphilitic chorea is, I feel quite sure that it is not so rare as to justify the almost total absence of all allusion to it in the works upon neurology, syphilis, and general practice. Instead of occupying your time with the long list of such works that I have consulted, I will endeavor to fill it more profitably by reporting a case of chorea in a congenital syphilitic which I was asked to see by Dr. S. L. McCreight, and by whose kindness I am permitted thus to bring before you:

H. P., male, aged eleven years, born at full term, of German parentage, and showing at present unmistakable signs of inherited syphilis. The family history is noteworthy. The father of the lad, now about forty years of age, married some fourteen years, admitted to his wife and earlier physicians that he had contracted syphilis about ten years prior to his marriage. Nine years ago he experienced his first apoplectic

attack, which involved the entire left side of his body and for a brief period his speech. The paralysis lasted twenty-eight weeks and then disappeared almost completely. A second stroke occurred five years ago, involving the same side. This attack was preceded by several spells of weakness, largely in the same extremities. This second attack lasted about two weeks. At this time he was blind for several weeks, but his eyesight underwent partial recovery. Maniacal attacks also took place, and the man was admitted into the County and Dunning Hospitals. These periodical attacks of mania, with intervening spells of quiet foolishness, lasted for some time, finally passing into dementia. At the present moment he is living at home, a sad picture of irresponsible, harmless dementia with paresis.

The mother of our patient is an exceptionally bright, active woman, without the slightest evidence of syphilitic taint. She denies having had any miscarriages. There are four living children, all of whom show more or less positive signs of syphilis. The eldest is twelve years of age; has been obliged to wear glasses since she was five years of age; is the victim of excruciating headache; exhibits every now and then a severe eruption of the skin; and suffers almost constantly from a sore throat. Mentally she is above the average and stands always at the head of her class in school. She has chronic nasal catarrh.

The second child is our patient.

The third child is not quite ten years of age; has marked ozæna; suffers from frequent skin eruptions; exhibits the Hutchinson teeth, and is the victim of frequent attacks of sore-throat. Seven years ago an ulcer-like eruption broke out behind the ear and spread around the neck to the back of the head.

The fourth child is five years of age; suffers from ozæna, skin eruptions, sore-throat, and troublesome diarrhœa.

Let us return now to our patient, the second child. He appeared to be healthy until he was about two years of age, when without warning he was taken with five severe convulsive seizures, one following the other in rapid succession, and all occurring within the space of a few hours. The mother supposed that these were simply attacks of ordinary infantile eclampsia, and so cannot give now any very clear account as to how they started, continued, or terminated. This is unfortunate and renders incomplete a most important part of the history. It was during these seizures that the boy's "eyes went wrong," in the phraseology of the mother, and left him with his present internal strabismus. Diplopia, of course, was present for a time, but now the vision of one eye is almost negative. It is important to remember this condition of the eyes when considering the chorea, though in this case I do not believe there was any causative relationship. The examination of the fundi a year or so ago by Dr. McCreight discovered nothing very abnormal. The shape of the boy's head and the development of his body show a condition of degeneracy. About three years ago the mother suspects that he had an attack of rheumatism with heart-failure. At present, however, there are no signs of organic heart disease. It is well known how syphilis of the central nervous system simulates almost all other diseases. Scarlet fever and measles are to be added to the history.

After the convulsions at two years of age, the left side became gradually and noticeably weaker and thinner. There has never been

any repetition of the convulsions. At seven years of age the boy suffered his first attack of chorea. It seemed to be slightly more obvious upon the left side than upon the right side. The attack, however, was of the generalized form. Four attacks have occurred altogether, about a year apart and each more severe than the previous one. Except the last one, they continued only a few weeks and then gradually disappeared. The movements were all irregular, spasmodic, and inco-ordinated. They were typically choreic and not slow and rhythmical as they are in the so-called "symptomatic" chorea of the writers. They were partially under the control of the will, and except upon the rarest occasions did not occur during sleep. They involved all parts of the body. The head, face, arms, and legs twitched constantly. It was quite impossible for the boy to hold a knife and fork, and at times the movements were so strong and violent as to throw him from the chair or couch. There was nothing of an athetoid condition about the movements. His last and fourth attack, which began about ten months ago, was the most severe of any and lasted altogether about four months. All the usual remedies for chorea had been tried and failed utterly to modify the choreiform movements. The patient's mental state showed a gradual weakening, and as a result of the constant jactitations there were signs of profound physical exhaustion. There is no cephalalgia. He complains of indefinable, shooting pains here and there about the body and a feeling of general soreness in the whole left arm. This soreness may be due in part to the muscular exhaustion.

Two weeks after beginning the administration of potassium iodide, there was a noticeable diminution in the jactitations and in a week or two more they had ceased entirely. At present the boy is perfectly well, except for a few feeble twitchings which occur at rare intervals. The unilateral character of these present movements is to be noted and their appearance almost always in that part of the body which showed hemiplegic tendencies.

This, then, was a case of what the authors call "symptomatic chorea," or, rather, generalized chorea with certain localized "symptomatic" manifestations, due to inherited syphilis. The nature of the lesion may be imagined, but cannot positively be defined.

Within comparatively recent times only has the so-called "symptomatic" variety of chorea, hemichorea, prehemiplegic and post-hemiplegic chorea been carefully studied and described by Weir Mitchell, Charcot, Hoffman, Jackson, and others. Perhaps the majority of the cases of choreiform convulsions due to syphilis of the central nervous system are of this class. Our own case, indeed, exhibited to a large extent this definitive localization of the movements. In these cases the movements are generally described as eccentric, with more or less tremor. They are slower, somewhat more rhythmical, and less brusque than they are in ordinary chorea. They are usually unilateral and depend in most of the cases upon a lesion in the pyramidal columns somewhere between the bulb and the cortex.

In our case, however, as well as in some others that have been reported, the movements were generalized and identical with those of

ordinary chorea. This at once raises the question as to the rôle of syphilis in the causation of Sydenham's disease and its *modus operandi*. In spite of the occasional embolic, hemorrhagic, and inflammatory findings, these lesions are not constant enough to form the basis of the pathogenesis of generalized chorea. Moreover, the very conception of the so-called "symptomatic" chorea would lead one to suppose that such lesions should give rise to symptomatic chorea only. This taken in conjunction with the fact that ordinary chorea so often follows infection, the view has come into prominence that Sydenham's disease is the expression of a toxic nutritional or molecular change in the cells of the cortex. This being so, it is not unreasonable to suppose that the toxin of syphilis can and does act like any other toxin in producing ordinary chorea.

Many reasons might be assigned why syphilis is not more frequently found as a cause of chorea. In the first place, syphilis is rare in childhood, and chorea or the susceptibility to choreiform manifestations seems to belong to the infantile nervous system. Even hereditary syphilis is rare as compared with some of the other infections known to produce chorea in the child. Jacobi quotes Starr to the effect that cerebral syphilis is very rare in childhood, and cerebral gummata are exceedingly scarce below the twelfth year of life. This alone will explain the infrequency of this cause of chorea. In the second place, it is a cause that until quite recently was not thoroughly sought for in all cases of chorea. And in the third place, it is possible that syphilis to be a cause of chorea may require a special neuropathic condition in the patient. All syphilitic children may not develop chorea any more than all syphilitic adults develop locomotor ataxia. There are no arguments against the possibility of syphilis being a cause of chorea; but, on the other hand, there are many in favor of it.

The authorities who omit all reference to syphilis as a cause of chorea far outnumber those who do make mention of it. A few references will serve to illustrate that even among those who do admit the possibility of the causative influence of syphilis, there is much hesitancy and not a little diversity of opinion.

In the *American Text-book of Genito-urinary Diseases* it is stated, under the heading Syphilis, that "mobile spasms, such as tremors, ataxic movements, athetosis, and chorea, have been observed to accompany syphilitic irritation of the motor cortex and also irritative lesions of the basal ganglia. Of course, these symptoms are unilateral and are observed on the side of the body opposite to the lesion."

Nothnagel mentions symptomatic chorea, and declares that it is very rare after syphilis.

Risien Russell, writing in Allbutt's *System of Medicine*, observes that measles, variola, diphtheria, enteric fever, cholera, pneumonia, and pertussis are followed by chorea. Pyæmia and gonorrhœa may give

rise to it. He makes no allusion, however, to syphilis. Further along he states that "chorea has appeared in the course of secondary syphilis, which disease Féré considers has been justly regarded as a causative factor."

Féré's own words in the *Twentieth Century Practice of Medicine* are: "Syphilis has likewise, and justly, been given as a causative factor of chorea."

Neumann, writing upon Syphilis for Nothnagel's *System*, refers to chorea, epilepsy, visceral neuralgia, and angina pectoris as among the neuroses of syphilis, and to be considered along with the hysteria and neurasthenia from the same cause.

Eichhorst, in his *Practice of Medicine*, article Chorea, says, in regard to its etiology "in adults, syphilis also is to be taken into consideration."

Diday and Sturgis, in their work upon *Hereditary Syphilis*, point out that chorea is one of the results of the inherited infection.

Besides those who do not mention syphilis at all as a cause of chorea, there are a number who take the position of Keating in his *Cyclopædia of the Diseases of Children*. After referring to a case of chorea with syphilitic hemiplegia, the writer states that the "relationship of cause and effect cannot be considered established."

It is obvious that a certain few authorities recognize the causative influence of syphilis in the production of a localized symptomatic chorea. They admit their belief that these cases may be the result of acquired syphilis, and that they are to be likened to the cases supposed to be caused by such gross lesions as emboli, minute hemorrhagic extravasations, and inflammatory foci. Still smaller is the number who are willing to admit the possibility of hereditary syphilis as a causative factor. And, finally, almost next to none commit themselves to the belief that the functional neurosis of ordinary chorea may be the result of a syphilitic toxæmia.

For my part, I cannot see why syphilitic toxæmia may not act as a cause in disturbing the nutritional function of the cortical cells and so produce ordinary chorea, if it is to be admitted that this form of chorea is a nutritional and functional disease. If it is only an irritative disease dependent upon gross lesions, then it is all the more probable that syphilis is a causative factor.

I would formulate conclusions about as follows:

1. Syphilis in rare instances is a cause of chorea, and should always be thought of as a possibility in the examination of every case.

2. Chorea may be the result of acquired or hereditary syphilis.

3. Most of the cases of syphilitic chorea are unilateral; belong to the prehemiplegic or posthemiplegic type of the disease; may or may not be associated with other signs of an irritative lesion; are not in-

frequently developed in hereditary syphilitics, and are to be attributed probably to a functional disturbance of an irritative sort in the cortical and ganglionic motor cells.

4. The existence and recognition of these two forms of syphilitic chorea—the focal and the generalized—support the inference that all forms of chorea are but the expression of one or more of a multiplicity of possible factors which may disturb the functional activity of the upper motor neurons, these factors being all the way from a gross lesion down to a molecular or chemical change not demonstrable with our present means of investigation. This conclusion leads to the further conclusion that chorea is not a disease, but a mere symptom.

5. Syphilis, when determined as the cause of a case of chorea, should lead to the prompt and thorough treatment of the case as one of syphilis and not chorea.

A BRIEF REPORT OF TWO HUNDRED AND TWENTY-SEVEN CASES OF PARESIS.

By Horace Phillips, M.D.,
of Philadelphia.

The number of patients admitted to the Pennsylvania Hospital for the Insane suffering with paresis during the past eighteen years was 227, of whom 197 were males and 30 females—a proportion of 7 males to 1 female, being about the same ratio in which the disease attacks the two sexes (8 to 1) as observed by continental writers.

The limits of age at which the disease develops is much alike in both sexes, the youngest male observed being twenty-six years of age, youngest female twenty-seven years of age.

The most advanced age in either sex being:

Males	67 years.
Female	52 "
Making the average for male	46 "
" " " " female	38 "

Taking the ages of occurrence by decades we find:

Males.		*Females.*	
20 to 30 years	3 per ct.	20 to 30 years	16 per ct.
30 " 40 "	41 "	30 " 40 "	56 "
40 " 50 "	41 "	40 " 50 "	23 "
50 " 60 "	13 "	50 " 60 "	5 "
60 " 70 "	2 "		

In this table it will be seen that the decades from thirty to fifty years in both sexes give the preponderance of the advent of the disease, the percentage during this period being:

Males	82 per ct.
Females	79 "

The decades before and after this period furnishing:

Males but	18 per ct.
Females but	21 "

NATIVITY.

Men.		*Women.*	
Native born	86 per ct.	Native born	90 per ct.
Foreign born	14 "	Foreign born	10 "

SOCIAL CONDITION.

Men.		*Women.*	
Married	63 per ct.	Married	73 per ct.
Widowed	7 "	Widowed	17 "
Single	30 "	Single	10 "

OCCUPATION.

Men.		*Women.*	
Mechanics	15 per ct.	Housekeepers	86 per ct.
Laboring classes	9 "	Saleswomen	10 "
Mercantile pursuits	65 "	Domestic service	4 "
Physicians	3 "		
Lawyers	2 "		
Military officers	5 "		
Civil officers	2 "		
Musicians	5 "		
Unascertained	2 "		

Males.		*Females.*	
The cause of the disease in which a history of intemperance was given	29 per ct.	Ill health and domestic affliction	60 per ct.
Ill health associated with overwork and anxiety	26 "	Intemperance	6 "
In which specific disease had occurred	16 "	Menopause	4 "
In which specific disease associated with intemperance	12 "	Unascertained	30 "
Traumatism	3 "	Heredity was found in	21 "
Insolation	3 "		
Unascertained	11 "		

TIME THE DISEASE HAD PROGRESSED PRIOR TO ADMISSION TO HOSPITAL.

Males.		*Females.*	
Under 6 months	34 per ct.	Under 6 months	23 per ct.
Under 1 year	14 "	Under 1 year	30 "
Over 1 year	30 "	Over 1 year	13 "
Under 2 years	17 "	Over 2 years	36 "
Over 2 years	33 "		
Unascertained	5 "		

DURATION OF DISEASE OBSERVED.

Males.	*Years.*	*Months.*
Average residence in hospital of patients discharged or removed	...	7
Longest period of residence of any case	3	...
Shortest period of residence of any case	...	1
Average duration of disease of cases which remained under treatment in hospital until termination of disease	1	8
Longest period of any case under treatment	5	9
Shortest period	...	1
Average period of duration of patients remaining under treatment at hospital	1	2
General average of duration of disease of all cases observed	2	...

Females.	*Years.*	*Months.*
Average residence in hospital of those discharged	1	7
Longest period of residence of any case	10	6
Shortest period of any case	...	1
Average period of residence of those who remained under treatment until termination of disease	2	3
Longest period of treatment of case.	11	...
Shortest period	...	1
Average period of duration of patients remaining under treatment at hospital	3	4
General average of length of duration of disease of all cases observed in hospital	2	9

Of the patients admited 3 per cent. were in the first stage of paresis.
" " " 89 " " second stage.
" " " 8 " " third stage.

Periods of remission from all active symptoms of the disease occurred in 9 per ct. of cases.
Convulsive seizure occurred during the progress of the disease in . 60 " "

TERMINATION.

Termination of paresis in death in convulsion occured in . . . 30 " "
Death as a result of exhaustion in . . . . . 70 " "

ARGUMENTS IN FAVOR OF THE EXISTENCE OF A SEPARATE CENTRE FOR WRITING.*

BY HERMON C. GORDINIER, M.A., M.D.,
OF TROY, N. Y.

No subject in neurology has attracted more attention or excited more discussion than agraphia; that is, whether or not the ability to write depends upon the integrity of a separate cortical centre near to, but absolutely distinct from, that of Broca's area, through which articulate speech is effected. Two diametrically opposed views are at present earnestly maintained. The first and older view is that a focal cortical centre for writing does not exist, and that the inability to write is as much the result of a lesion of Broca's centre as is the inability to speak. A lesion of this centre, therefore, always excites motor aphasia or agraphia. This is the one advocated by the earlier observers—Trousseau,[1] Gairdner, Wernicke, Lichtheim, and Hughlings Jackson—and now strenuously supported by Dejerine, Mirallie,[2] and Wyllie, in Europe, and Collins[3] in America. The second view, on the contrary, maintains that the act of writing is independent of the faculty of expression by articulate speech, and its loss is due to the destruction of a cortical centre, distinct from the motor speech or arm centres, and its seat is probably located at the base of the second left frontal convolution. The supporters of this view believe that agraphia does occur as a distinct entity; that it may be unaccompanied by motor aphasia, and that when the two defects occur together both the motor speech

* Read at the Annual Meeting of the New York State Medical Society, January, 1903.

and the writing centres or the association tracts connecting these centres are involved.* This view is supported by Exner, Marcé,[4] Ogle,[5] Charcot, Kussmaul, Oppenheim,[6] Bastian,[7] Beevor,[8] Bramwell,[9] and Collier, in Europe, and Eskeridge, Pershing,[10] Mills, Fränkel, and the author,[11] in this country. In support of this view, I have the following propositions to offer, with the discussion of each in their order:

First, that sufficient clinicopathological data exist to show that motor aphasia and agraphia do not necessarily exist together, and that complete destruction of Broca's centre does not necessarily cause agraphia.

Second, that when motor aphasia and agraphia coexist, the lesion probably involves the bases of both the second and the third left frontal convolutions in the right-handed or the association tracts connecting these centres with the visual or auditory word areas.

Third, isolated motor agraphia, though exceedingly rare, does occur and depends upon a lesion of the base of the second left frontal gyrus in the right-handed.

In connection with the first proposition, it is very interesting to introduce Trousseau's own words in reference to the subject. He says: "The inability to write is proportionate to the inability to speak. Aphasics write as badly as they speak, and those who do not speak at all are absolutely incapable of writing." Marcé, on the contrary, in 1856, stated that "the centres of co-ordination for spoken and written words are different and separated from each other in position, since twice the patients could write freely when they were quite unable to speak. It is independent of the mobility of the hand, since when the hand has preserved all its powers writing has been found to be impossible."

In support of the first proposition and to show the fallacy of Trousseau's reasoning, I will introduce abstracts of the following cases, one of the most typical of which was Trousseau's own case.

He tells of a robust young civil functionary who, in an attack of unconsciousness, had entirely lost the power of speech. There was no paralysis of any parts of the body. He could execute all the movements of the tongue and lips with the greatest facility. He was able to discharge the duties of his office, notwithstanding the loss of speech, as he could transact all his business in writing. He delivered to Trousseau an exhaustive history of his case which had been written out by himself.[12]

Oppenheim[13] reports another interesting case of a painter, who for seventeen years following an apoplectic attack was completely aphasic

* Dr. Beevor states in a personal communication that his case is one of pure motor agraphia with slight right-sided hemiplegia unaccompanied with aphasia, word-blindness, or word-deafness.

and could utter nothing save the words "yes" and "no," but could give a written account of his entire illness and could paint beautifully.

Idelson,[14] Oppenheim's assistant, has recorded a case of a patient who had been cured by inunctions from a left-sided hemiplegia, hemianopsia, and hemianæsthesia, who after a new attack became completely aphasic and was not able to utter a single word or syllable, but was able to write perfectly during his entire illness.

Charcot,[15] records the case of a woman who was under his care at La Salpêtrière. She had been seized with aphasia, but there existed no trace of paralysis, either of movement or of sensibility. In his patient aphasia was the sole morbid symptom, and atrophy of the left third frontal convolution was the only lesion revealed by the autopsy. This was believed to be due to an old occlusion or narrowing of the external and inferior frontal branch of the middle cerebral artery.

Bramwell,[16] in the *Lancet*, May 22, 1897, describes a case in which acute softening, confined to Broca's convolution, produced complete motor aphasia with little or no agraphia. The absence of any marked agraphia, according to Bramwell, was forcibly illustrated by the fact that the patient, who was unable to answer questions in vocal speech, carried a note-book about with him for the purpose of answering questions and carrying on a conversation in writing. Bramwell explicitly states that the case seemed totally opposed to the views to which the great majority of authorities on aphasia held, that destruction of Broca's convolution necessarily produces agraphia and that, as Gairdner long ago argued, the degree of agraphia is usually proportionate to the motor aphasia. It seems to support the view advocated by Bastian, which he also, independently, arrived at, *i. e.*, that the nervous impulses which set the motor writing centre into action do not necessarily pass through the motor speech centre in order to reach the writing centre, and that destruction of the motor speech does not usually give rise to agraphia.

Prof. C. K. Mills has sent me the notes, with photographs of the brain, of a very interesting case, supporting the theory of the dissociation of agraphia from motor aphasia. The lesion, as the photographs show, was limited to Broca's convolution.

Referring to his case, he says: "The main features of this case are as follows: The patient, after an apoplectic seizure, developed a peculiar form of aphasia, apparently without any preceding paralysis or any other symptoms of focal lesion like visual blindness, hemianopsia, etc. When examined by me about nine years after the onset of the aphasia, he had almost complete inability to name persons and objects which he was able to recognize through all his special senses. He had also a marked form of paralexia or paranomia. When he attempted to read, although he understood what he was reading, he

repeated an absurd formula of a few phrases. He had limited spontaneous speech, even using short sentences without concrete nouns correctly. He could write many single words correctly, sometimes misspelling, however. He held his pen or pencil correctly and wrote such words as he did write with ease and firmness. He was not a motor agraphic."

Ogle,[17] Bastian,[18] and Dickinson[19] have each reported cases in which there was right hemiplegia and aphasia, though the patients could write with their left hand. Ogle's case came to autopsy and showed a patch of softening involving the left frontal convolution and reaching downward and backward to the fissure of Sylvius. The second frontal gyrus was normal.

I will refer, briefly, to a case recently under my care, of a boy who entered the Samaritan Hospital, suffering from a depressed fracture of the frontal bone. He had several attacks of unilateral spasms of the face and complete aphasia. The depressed bone was elevated and several blood clots removed, but the aphasia remained. He nodded assent or dissent when spoken to, recognized objects, and seemed to understand, perfectly, printed or written language. There was no hemianopsia or paralysis of either arm. He was able to write his name the day following the operation and in a few days he wrote sentences, copied, and wrote correctly from dictation.

Altogether the most remarkable case on record to disprove the views of Trousseau, Dejerine, and their followers, is the one recorded by Guido Banti.[20] It will be reported here in full. A right-handed man, aged thirty-six years, who was able to read and write correctly, had a sudden apoplectic attack in 1877. Recovering consciousness in a few minutes, he was found to be suffering from right hemiplegia and loss of speech. The paralysis of the limbs disappeared the following night, although the inability to speak remained. The next day he was admitted to the hospital, and after a most careful examination, his condition was found to be as follows: The mobility of the limbs on the right side had returned to their normal condition. There was no trace of paralysis of the face or tongue. The patient made ineffectual attempts to speak, but he could not articulate a single word, not even isolated syllables. He was much affected by his mutism and sought to make himself understood by gestures. When given the necessary articles and when asked to write his name, he did it immediately. Other questions were put to him to which he replied in writing. He wrote the details and description of his illness without hesitation. Various objects were shown to him, such as pieces of money, etc., and he answered, correctly, the name of each object in writing. Then instead of giving him directions by word of mouth, I wrote them for him, in order to thoroughly convince myself that he was able to under-

stand writing. He replied to these questions with perfect correctness. He wrote very rapidly and did not seem to hesitate for words. He made no mistakes in syntax or orthography. He could understand, equally well, ordinary writing and print, and when one spoke to him he grasped their meaning at once, and never wished to have their questions repeated. Banti wrote some simple words and asked him to repeat them aloud. This he could not do. He then pronounced some words and asked him to repeat them after him. He watched the movements of my lips and tried very hard to obey, but he never succeeded in pronouncing a single word. The patient died in February, 1882, from an aneurism of the aorta. At autopsy a patch of yellow softening was found, situated in the posterior third of the left third frontal convolution.

In summarizing the ten cases above narrated, we find that complete motor aphasia occurred in each without agraphia. In five of the cases no autopsies were had, but in each of these cases the clinical history was very plain, and there was no paralysis of the muscles of either hand. In five of the ten cases autopsies were had, namely, those of Charcot, Ogle, Banti, Bramwell, and Mills. In Charcot's case the pathological lesion was an atrophy confined to the left frontal gyrus, due to occlusion of the inferior branch of the Sylvian artery. The only symptom was complete motor aphasia. In Ogle's case the third left frontal convolution was softened, while the second left frontal convolution was found normal, and there was motor aphasia without agraphia. Banti, in his case, found as the only lesion an area of softening limited to the posterior third of Broca's convolution, involving only the cortex. This had caused in a right-handed person, perfectly able to read and write, motor aphasia without agraphia, there being no word deafness, alexia, or hemianopsia. In the very carefully reported case of Bramwell, softening limited to Broca's convolutions produced complete motor aphasia with little or no agraphia. In Mills' cases the lesion was confined to Broca's area and still there was no motor agraphia. Collins, in his recent work on *The Faculty of Speech*, p. 177, makes the following statement: "A patient with cortical motor aphasia is completely agraphic, never learns to write with his left hand, no matter how long he lives after the aphasia develops." This statement seems too sweeping, as the first part of the statement is disproven by the autopsies of the cases of Charcot, Banti, and Bramwell, and the latter part, particularly, by the case of Ogle.

These cases, it seems to me, prove beyond a reasonable doubt, that motor aphasia and agraphia are due to two distinct lesions, and may occur disassociated. They also prove that motor agraphia is not usually a symptom of a lesion limited exactly to the cortical area of Broca.

The cases reported by Broca, Tamburini,[21] and Marchi,[22] together with the notes of an unpublished case, with autopsy, sent to me through

the courtesy of Dr. John K. Mitchell, of Philadelphia, furnish very strong evidence in support of my second proposition; that is, when motor aphasia and agraphia coexist, the lesion probably involves the bases of the second and third left frontal convolutions. In each case above referred to, the symptom-complex—motor aphasia, with agraphia unaccompanied with hemianopsia, alexia, or word deafness—was present. The cases of Broca and Mitchell are of such great importance in this connection that I will give a short *résumé* of each:

Broca's case, a man aged eighty-four years, came under his care October 27, 1861, with the following history: In April, 1860, he had a slight apoplectic attack, from which he recovered in a few days. No paralysis of the limbs occurred, but his speech was lost, save for four or five very simple words. His intelligence appeared normal. He understood all that was said to him and he made use of expressive gestures. He had been in this condition eighteen months prior to Broca's observation of him. To his questions he was able to reply only by signs accompanied by one or two syllables pronounced hastily and with much effort. Broca asked him to write and, although his arm and hand were not paralyzed, he could not write a single letter. His sight and hearing were good. The tongue was protruded straight and was movable in all directions. The patient died November 8, 1861. At the autopsy the lesion, an old hemorrhage, was exactly limited to the posterior third of the second and third of the left frontal convolutions. This hemorrhage was, doubtless, the cause of the apoplectic seizure which occurred eighteen months before, as the brain showed no other lesion.

Dr. Mitchell's case was a man, aged forty-four years, who was highly intelligent and well educated. His brother died of sarcoma of the brain. He had headaches for ten or twelve years, which were attributed to eye-strain. These headaches have greatly increased for the past two or three years. In August, 1899, he had an attack of difficulty in articulation, with numbness of both hands, but no loss of power. The attack lasted ten minutes. Three weeks later there occurred incoherent speech and violent twitchings, first of the right and then of the left side of the face. Later on, similar attacks appeared, which in one or two instances were followed by a semicomatose state lasting twenty-four hours. The headaches increased to an unbearable degree. In February, 1900, optic neuritis appeared. Up to this time a tumor seemed doubtful. In several attacks he had temporary loss of speech, followed by impairment of articulation, but with the consciousness of his loss of power of formulated speech slight enfeeblement of the right arm was noted. His difficulty in writing was precisely similar in character to his difficulty in speaking.

At the operation a large endothelioma, measuring 7 cm. by 8 cm.,

was removed. He died two hours after. The upper third of the ascending frontal and the highest part of the superior frontal gyri were not compressed by it. The lower posterior portion of the superior frontal and the whole of the posterior portions of the middle and inferior frontal convolutions, the lower two-thirds of the ascending frontal, except the extreme lowest part, were all compressed beneath it. The tumor did not extend beyond the fissure of Rolando and did not invade the brain tissue, but started apparently from the dura, pressed upon and caused thinning of the cortex and localized atrophy of the cerebrum. Autopsy and notes were made by Dr. W. G. Spiller.

The four cases above mentioned are the only ones in literature with which I am acquainted that present, clinically, motor agraphia and motor aphasia with the pathological lesion at the base of the second and third left frontal convolutions. In Broca's case there were no other symptoms present, save the inability to write and to speak, and the lesion was limited exactly to the bases of the left median and inferior frontal convolution. In Dr. Mitchell's case, the lesion, a tumor springing from the dura, involved these same-named gyri by the constant pressure causing a thinning and atrophy of the cortex without involving the white matter. The symptoms present, apart from a very slight weakness of the right arm, were motor aphasia with agraphia, and the inability to write, corresponding exactly to the inability to speak. It would be impossible to explain away these cases on the supposition of a subcortical aphasia, the lesion being so placed as to interrupt the association tract connecting the visual word area with the motor speech, or, more properly, motor writing centre, thus placing the agraphia in the category of a sensory type.

In none of the cases was hemianopsia, word deafness, mind blindness, alexia, motor or sensory paralysis present. These cases, therefore, support the theory of the separate existence of a writing centre located at the base of the second left frontal convolution.

Drs. Fränkel and Onuf,[24] from a study of 104 cases of motor aphasia with autopsies, conclude that the function of writing is independent of Broca's area, and the presence or absence of the act of writing is of no value in differentiating a subcortical from a cortical motor aphasia.

To verify my third proposition, that isolated motor agraphia, though exceedingly rare, does occur, and depends upon a lesion at the base of the second left frontal convolution in the right-handed, I direct your attention to the cases of Pitres,[24] Charcot and Dutil,[25] and Eskridge,[26] together with my own case of a glioma at the base of a second left frontal convolution, the only localizing symptom present being complete motor agraphia uncombined with any form of aphasia, in a right-handed person, without paralysis or hemianopsia.

In Pitre's case the intelligence was normal; there was paralysis of the right side without anæsthesia, which soon disappeared; there was no trace of word deafness or word blindness; nevertheless, the patient was incapable of writing spontaneously or from dictation, but could copy in fac-simile. This condition existed ten years. He had hemianopsia and was able to write with the left hand. Those who would give no credence to this case because of the presence of hemianopsia explain the loss of writing on the supposition of a subcortical lesion interrupting the association tract between the left angular gyrus and the motor area of the left side. While any explanation of the case without post-mortem evidence is purely speculative, the clinical symptoms certainly place it in the category of a partial motor agraphia. A subcortical lesion so placed as to produce hemianopsia and sensory agraphia must, necessarily, have destroyed the optic radiations as well as the fibres connecting the angular gyrus with the motor zone, and because of its size produced word blindness or alexia. The clinical record shows that word blindness did not exist and that the patient was able to copy in fac-simile. I have been able to find but six cases, with autopsies of sensory agraphia, all of which were accompanied with blindness or alexia.

The case of Charcot and Dutil was that of a woman who, after her first apoplectic attack, had no symptom except motor agraphia. Years later, a second attack left motor aphasia. After repeated attacks there developed pseudobulbar paralysis. There was no word blindness or deafness. At the autopsy a focus of disease was found in the foot of the second left frontal convolution, another at the foot of the third left frontal convolution, and three in the middle of the right hemisphere. This case seems perfectly simple if we could but prove that the oldest focus of softening was at the base of the second left frontal convolution, as the clinical symptom—motor agraphia existing alone so long a time—would indicate. The presence of agraphia for years before motor aphasia occurred certainly stamps the case as one of pure motor agraphia.

The case described by Eskridge had no paralysis of motion or sensation; no sensory aphasia. His power of articulation was perfect, except a little slow. He could talk, read printing or writing aloud or to himself, and understood what he read. There was no difficulty in propositionizing, and the movements of the lips and tongue were preserved except in uttering very long and hard words. Otherwise it was impossible to discover any speech defect. In writing he formed letters properly, but transposed letters, words, phrases, and sentences, so that it was quite impossible to read what he had written. Formerly he had been an expert penman. He was observed for two months and he tried to write a letter daily, consisting of a few lines. He spent

two hours or more in writing or erasing words, before he could finish the assigned task. At times he seemed to recognize his mistakes in spelling, and at other times he did not recognize them and was indifferent to them. In trying to correct his errors he would usually make a greater one. At the operation a cyst was found at the base of the second left frontal convolution, which had destroyed the cortex over an area of about half an inch in diameter and had extended into the white substance. After the operation his writing improved very rapidly.

According to Dejerine and Collins,[27] the ideal case to prove the existence of a centre whose function is to store graphic images, and whose destruction would cause agraphia, would be one in which there was inability to write spontaneously and from dictation, and in which no disturbance of motility, particularly no disturbance of the right upper extremity, no aphasia, no alexia, no verbal deafness, and no verbal blindness existed. Collins states "that if anything is needed to make the data of aphasia more reliable in the future and more utilizable as scientific evidence in support of or in behalf of certain theories of the genesis of speech and localization, it is that the patient be studied methodically and carefully, and, when the case comes to autopsy, that the findings be recorded in scientific language, particularly the seat, extent, and nature of the lesions. A study of subcortical lesions to be of much value must be done with the microscope."

Both conditions, I submit, are fulfilled by my case, the notes of which are as follows:

The patient, Mrs. L. W., an intelligent Irish woman, received her education in the public schools. Her age was thirty-seven years, and she had been married for fifteen years; had had five living children and one miscarriage at the third month. Her father died at the age of sixty years, of cancer of the face. Mother alive and in perfect health. Has a brother and a sister living and in good health. Has lost two sisters, one of Bright's disease, the other from consumption. The patient had always enjoyed excellent health up to the onset of the present illness, which began about Christmas, 1897, when she began to fail in strength and had several attacks of vertigo, without falling and unattended with nausea or vomiting. A short time afterward she developed severe frontal and occipital headaches, with an occasional attack of vomiting. The headaches continued with increasing severity until the fatal issue. In March, 1898, she noticed that her sight was failing and that she could not read print without the use of glasses. At about the same time she began to complain of a numbness in the right arm. At no time during her illness did she have a unilateral or general convulsion. Her bowels have been rather constipated. She has had perfect control over her bladder. Has menstruated regularly and in a normal manner. Patient converses intelligently, makes no errors, and her memory for past and recent events is good. At no

time during illness has she had the slightest difficulty in giving expression to her thoughts by articulate speech.

Examination, April 5, 1898. Patient 5 feet 4 inches in height; weight, 140 pounds. Physical examination of the chest and abdomen elicited nothing abnormal. Urine normal. Temperature 98.6° F., pulse 68. Head well formed and perfectly symmetrical. No evidence of previous injury; no exostosis. Percussion of scalp elicits no tenderness. Veins of forehead not prominent. Pupils moderate and equally dilated, and respond actively to light and accommodation. Wernicke's hemianopic pupillary phenomenon not present. No hemianopsia. Optic neuritis of both eyes, though more intense in right eye. Owing to paresis of the right external rectus muscle, the right eyeball could not be rotated outward, but its movements upward, downward, and inward were found normal. Diplopia existed. Excursion of left eyeball normal. Color vision normal. Drum membranes appeared normal. Hearing distance for watch in each ear was three feet. Movements of tongue normal. No fibrillation or atrophy. Sense of taste and smell normal. Soft palate and uvula move in a normal manner. No loss of sensation over buccal or pharyngeal mucous membranes. Movements of vocal cords normal. No difficulty in swallowing. No stiffness of neck muscles or those of the spine. Both sides of the face symmetrical. No evidence of facial paralysis. Patient is able to perform, in a normal manner, symmetrical bilateral movements. Grip of right hand is slightly weaker than that of left. Dynamometer: outer scale, right, 50; left, 75. No muscular atrophy anywhere discoverable. No stiffness of muscles. Fine and coarse movements of both hands and arms normal. Movements of lower extremities normal. Muscular power of both legs equal. The most careful examination of the skin of the entire body showed no sensory disturbances. No œdema or other vascular changes. The most careful reinforcement failed to elicit the presence of patellar tendon reflexes. No ataxia in upper or lower extremities. The sense of posture normal. Romberg's symptom absent. Gait perfectly normal. She has always been right-handed.

Speech. Patient recognizes and names correctly any object placed before her. She can recognize and accurately name, with her eyes closed, any familiar object when placed in her right hand, such as coins and the like. She understands perfectly what is said to her. She recognizes familiar hymns. She can repeat words after another and speak voluntarily without the slightest hesitation, and always correctly. She can read correctly, with the aid of glasses, ordinary sized print or writing. She recognizes numerals at once. The only difficulty present is the total inability to write. Although she understands perfectly written language and can read to herself or aloud, she cannot write, voluntarily, nor form, correctly, a single letter, and cannot write from dictation or copy. She holds the pen in a perfect manner, and performs movements with it as if to write. Her writings consisted, however, of nothing more than a series of united curves. She was unable to write with her left hand, as she was not ambidextrous. The fine and coarse muscular movements of the right hand are executed in a perfect manner, and there exists no paralysis of the muscles of the hand, forearm, or arm. Before the present illness began, she could write perfectly. She showed me some of her writing, which was excellent.

Without the slightest external manifestation of a syphilitic infection, it was thought wise to give the patient the benefit of the doubt, and hence potassium iodide combined with mercury was administered for six weeks.

May 20th. After six weeks' continuous use of increasing doses of potassium iodide combined with mercury it was discontinued, there having been no amelioration of any symptom. No sensory or motor symptoms. No hemianopsia or alexia. Voluntary speech perfect. Cerebration, which was very active at my first examination (the patient answering the numerous questions put to her very quickly and correctly), was now quite slow. This slowness of speech was not in any sense aphasic in character, as all questions were answered correctly, only there was considerable deliberation before the answers came. Memory good. There is an absolute inability to write voluntarily from dictation or to copy. The patient holds the pen or pencil in perfect position and the movements of the forearms and hands are normal. Has perfect control of sphincters. In no other particular was her condition different from that noted above, save that there is a tendency to fall or to stagger toward the right side. This ataxia did not exist at the date of the first examination. The patient has noticed this condition for about three weeks, and she thinks it is becoming gradually worse. It is an inco-ordination similar to that of cerebellar disease, and is like that frequently observed in disease involving the prefrontal lobe.

This condition of complete agraphia continued throughout her illness and was, with the exception of a gradual development of a slow cerebration and frontal ataxia (Bruns), the only localizing symptom present. At no subsequent time was there found the slightest evidence of motor or any form of sensory aphasia. She never had a partial or complete unilateral or general convulsion, never became paralyzed or developed any sensory disturbance. Hemianopsia or alexia were never present. The presence of agraphia without motor aphasia, with a gradually increasing slow cerebration and ataxia, coupled with double optic neuritis, with severe and continuous headaches, unaccompanied with alexia, led to the diagnosis of a lesion of the prefrontal lobe, probably a new-growth, the situation of which I was led to believe, owing to the fact that the slow cerebration and inco-ordination developed subsequently to the agraphia, was at the base of the second frontal convolution of the left side.

After six weeks of further suffering, there being no change in her symptoms, she consented to an exploratory operation, which was performed July 19, 1898, by Dr. E. D. Ferguson, of Troy, N. Y. The left Rolandic area was exposed after the method of Reid, under strict asepsis. The trephine opening was next made through the middle third of this area. On removing the button of bone the dura bulged into and through the opening, forming a very elastic swelling which pulsated feebly. On incising the dura there was an escape of a considerable amount of subarachnoid fluid, followed immediately by the formation of a troublesome hernia cerebri. The opening was now enlarged forward by the rongeur forceps, and a careful search was made for a lesion, but none was detected. The cortical area, exposed by trephine opening, appeared normal. While discussing the propriety of enlarging the opening still more forward, her condition became so

alarming that it was decided to close the opening at once. The vessels having been secured, the wound was closed with kangaroo tendon and a gauze drain was left in the most dependent part.

July 20, 1898. On awakening from her etherization, it was discovered that her right arm was paralyzed. She appeared very drowsy and stupid, and complained of great pain in the region of the wound. She was unable to move the right arm, and the movements of the right leg were impaired.

21*st*. Patient rapidly passed into a condition of unconsciousness. No control over bladder. Pulse rapid and very feeble. Temperature 101° F. She died at 4 P.M.

Left cerebral hemisphere, showing exact location and size of tumor producing motor agraphia in Dr. Gordinier's case.

Autopsy, July 22, 1898, at 10.30 A.M. Only the head permitted to be examined. Trephine opening, 4.5 cm. by 4.75 cm. Elevation of hernia cerebri above dura, 2 cm. Dura everywhere free. Superior longitudinal sinus contained a soft, recent thrombus. Vessels of pia injected. Left cerebral hemisphere: Marked hemorrhagic softening of the hernia cerebri and surrounding brain tissue. Pia not adherent save at location of the new-growth, which was found occupying the foot of the second left frontal convolution, being distinctly separated from the arm area by the precentral sulcus, which sulcus in this case was unusually well defined. The growth was elevated about 0.5 cm. above the surrounding cortex, was slightly irregular in outline, of a distinctly firm consistency, and oval in shape. Its longest cortical diameter was 2 cm. The pia was intimately adherent to it. On section, the tumor was seen to extend downward and inward in the centrum semiovale as far as the roof of the anterior cornu of the lateral ventricle, and forward to near the apex of the frontal lobe, involving almost exclusively the white matter of the second frontal gyrus. The left third or inferior frontal convolution through its whole extent was found (macroscopically) perfectly normal, as was its associated centrum ovale. The centrum ovale of the superior first frontal convolution

was, toward its ventral part, infiltrated by the growth. The motor convolutions in their middle third formed a part of the hernia cerebri. This area was filled with minute capillary hemorrhages, the result of the sudden relief of the intercranial pressure. The rest of the motor area and the underlying white matter was found normal. The supramarginal and angular gyri, with their associated white matter, was very carefully examined and found normal, as were the convolutions and white matter of the occipital and temporal lobes. The basal ganglia and the internal capsule showed no naked-eye changes. The convolutions, centrum ovale, basal ganglia, and internal capsule of the right cerebral hemisphere normal. The interior of the skull was found normal.

Histological Examination. The histological examination of the tumor showed it to be a glioma of rapid growth. It was of a yellowish-gray color, rather firm in consistency, not very vascular, and was inseparably blended with the surrounding white matter. It presented no softened areas, and there was no softening of the white matter in advance of it. It was not at all cystic in character. Sections of the tumor were placed for four days in Orth's fluid and subsequently hardened in alcohols of increasing strength. Small cubes were embedded in celloidin and stained with hæmatoxylin and eosin, Von Gieson's picric acid, fuchsin and hæmatoxylin, Weigert's myelin stain, and with Mallory's phosphomolybdic acid, hæmatoxylin, and phosphotungstic acid hæmatoxylin.

Microscopic examination of the left inferior or third frontal convolution, with the associated white matter, showed it to be normal.

The ventricles contained an excess of fluid. The brain stem, pons, cerebellum, medulla, and the cranial nerves showed no macroscopic changes.

This case seems to prove the existence of a separate and distinct cortical centre for writing, having the same relation to writing movements as the motor speech centre has to speech movements. This centre is located at the base of the second left frontal convolution for the right-handed, and probably in the same location in the right hemisphere for the left-handed. Destruction of this centre produces pure motor agraphia without aphasia or paralysis of either arm.

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A CONTRIBUTION TO THE SURGERY OF THE BRAIN, WITH THE REPORT OF TWO CASES OF TUMORS OF THE CEREBELLUM WHICH WERE LOCATED AND ON WHICH OPERATIONS WERE PERFORMED.

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Case I.—*Cyst of cerebellum located in the right lobe, in which two operations were performed, with ultimate recovery.*

History. Julia R., aged nine and one-half years. Family history good. Father healthy, strong, and well nourished. Mother very healthy and strong. The patient was one of twins, the other dying at birth. Both had supernumerary little fingers. The brothers and sisters are all in perfect health, the youngest children being twins, also with supernumerary little fingers. Father by a previous marriage had several children, two of the daughters dying of rapid pulmonary tuberculosis during the winter of 1894–95. The other children by the former marriage are healthy and apparently not tuberculous. The two daughters who died of phthisis lived in the same house with the family.

The patient, up to the summer of 1895, was very healthy and active. She was well developed and strong, and the brightest of the children. During the summer she began to complain of headache, which she said was in her eyes and forehead; it was occasionally so severe as to cause her to cry. Toward December these attacks became very frequent, and compelled her to remain in the house most of the time. The location of the pain was changed, and was now in the back of the head, and down the back of the neck, on the right side. During this period she vomited occasionally, always just as she got out of bed in the morning. She did not complain of nausea, but had frequent attacks of vertigo, which she called "swimming in the head." These attacks were usually in the morning when she was getting up. Her parents do not remember having noticed any clumsiness or staggering during this time; but from being the errand girl of the household, she became inactive and disposed to lie in bed. When not suffering, her parents thought her mind was as active and bright as it had ever been.

During the month of January, 1896, Dr. B. F. Rae, Jr., of Lafayette, was called to see her. He found it necessary to give her morphine to control the pain in the head. He noticed that her gait was staggering and that her eyesight was defective. He did not examine the optic disks. Dr. Rea saw her frequently during the winter and early spring months, and suggested the probability of a brain tumor. In May I saw the case with him, with a view to an operation if I could satisfactorily locate the tumor.

When I first saw the patient she was a well-nourished, healthy-looking girl. Her head was large, measuring twenty-two inches in circumference. Her eyes were very prominent and protruding, and, at every effort to move them, oscillated from side to side. She could not count fingers accurately, but could see your hand and could point out the doors and windows. The movements of the eyes were restricted in all directions. The abducens of the right eye was more defective than the other ocular muscles. She could close her eyes only when an effort was made, and could keep them closed only for an instant. Her mother said she had not closed her eyes when she slept for some months; that several weeks ago her eyes were so badly crossed that she could only see the "whites of the eyes," and since that time her eyes had been "rolling in the head all the time." The pupils were widely dilated and did not react to the light.

There was paresis of the right facial nerve, noticeable when she showed her teeth and when she smiled. There was no disturbance of sensation on any part of the face or neck. The tongue was protruded in a straightforward manner, and moved freely from side to side. Swallowing was not interfered with. Hearing was good and the same in both ears. Taste and smell were normal. The pulse was 65 beats to the minute and the respiration 18 to the minute. She never lost her appetite except during the time of intense headache, and at times it was voracious.

The patient was suffering with headache of moderate severity, located in the back of the head, and neck on the right side. The muscles of the neck were stiffened, and the head was slightly retracted. Her mother informed me that frequently when she awoke in the morning her head was drawn far back, and that it would take several hours, with "hot applications and rubbing" before she could "straighten her neck." She complained of severe pain in the neck when I attempted to lift her head.

There was no pain on percussion with a rubber hammer, but pain was elicited by firm pressure over the right occipital region, especially over the right cerebellar fossa. The grasp of the left hand was much weaker than the right, and the left leg was much weaker than the right. Both knee-jerks were totally absent.

As the patient lay in bed she could move her arms and legs freely, and, with the exception of the weakness in the left side, there was no marked deficiency in them. Co-ordination was good except to the fine tests. When she attempted to sit up her power of maintaining an equilibrium was markedly disordered. She could sit in a chair by using great care, but usually she held to the sides or the arms with her hands or leaned hard against the back. She did not appear comfortable sitting up, and evidently preferred lying in bed, where she stayed most of the time. When asked to walk she attempted to do so, but

with some reluctance, usually falling as she got up from the chair, or as she got out of the bed. When assisted to her feet and steadied she would walk forward six or eight feet and then gradually turn to the left, going, as she turned, three or four feet farther; here she would fall unless caught. Her gait was staggering and uncertain, but she would usually go the above specified distance before falling. When she turned around she would walk back in the same manner, turning toward the left and falling as before. One cannot say that the falling was constantly in a certain direction. When asked to stand, which, by your aid, she could do, and occasionally without aid if slow and careful in her movements, a vibratory action would pervade the muscles of her whole body, especially marked in the muscles of her trunk; then after an instant she would sway to and fro, and then lose equilibrium entirely and fall. She did not have the characteristic "saddle-back," but there was a slight forward turn to the pelvis, and the trunk stood above the pelvis in a very tottering, uncertain fashion, suggesting at once that the muscles of the back were much weaker than the muscles of the legs. I further tested the muscles of the trunk by placing her flat on the abdomen on a table; she could raise her head and shoulders only a short distance above the table; turned on her back, this defect was equally marked. As a control experiment, I compared her in these movements with her healthy sister of near her own age, and the difference was very perceptible.

There was intense optic neuritis in both eyes. The disks were concealed by a very prominent swelling with a central depression. The veins were enlarged and partly obscured in the swollen disks. The arteries were not seen until the edge of the swelling was reached. There were hemorrhagic points in the right eye. The loss of sight had occurred in both eyes at about the same time.

Recently the headache had grown less severe, and the vomiting had entirely ceased. The patient complained less frequently of vertigo. Her parents thought her mind was not as good as it had been. She kept her bed most of the time.

During the following twenty days I saw her frequently. The headache diminished until she ceased to complain of it, or rather she became so apathetic as to cease to recognize the pain. She became more stupid; at times her mind wandered. She lost strength in her legs, and there was a marked loss in her ability to walk. Instead of turning to the left on attempting to walk she would turn shortly to the right, making irregularly the segment of a small circle. This turning to the right was as constant as the turning to the left had been when I first saw her. Toward the last her legs became so weak that she could not stand. She lost control of the sphincters, her mind was rapidly failing; in short, all of her mental faculties were rapidly becoming "blotted out." Her mother was very emphatic as to her head having grown very rapidly recently, and called my attention to this fact of her own accord. I examined her head by percussion according to Macewen, and found the percussion note altered from that of health, the resonance being greatly increased, indicating that there was much ventricular distention.

The headache, vertigo, vomiting, and staggering; the paresis of the muscles of the trunk; the optic neuritis coming on early in both eyes and producing blindness; the hemorrhagic points in the retina; the

failure of mind, the prominent eyes, the nystagmus, and the increased resonance on percussion over the ventricles suggested a tumor in the cerebellum. The late appearance of staggering as a symptom in the disease and the paresis of the right facial and right abducens nerves, the tenderness to firm pressure over the right cerebellar fossa, and the weakness of the left arm and leg indicated with reasonable certainty that the tumor was located in the right cerebellar lobe, implicating the middle lobe by extension or by pressure. The freedom of the other cranial nerves indicated that the tumor was not at the front of the cerebellum, and probably accessible.

Of the nature of the lesion I could form no satisfactory opinion, although the great frequency of tuberculous growths in this part of the brain, and her exposure to tuberculous surroundings in the beginning of her sickness, led me to believe it probably tuberculous. She did not, however, present any signs of tuberculosis, but was remarkably well nourished. A glioma or a gliosarcoma was quite as probable.

Operation. On June 15th I operated under ether narcosis.[1] Before the operation Dr. Hilt was requested to be prepared to make artificial respiration should the breathing fail during the operation. The incision was made from a point midway between the left mastoid process and the external occipital protuberance just over the superior curved line, extending from this point about one-half an inch above the superior curved line of the right side to a point near the tip of the right mastoid process. The incision was not made with one sweep of the knife, but in sections of about two inches each, all hemorrhage from each section being under control before the next section was made. Instead of cutting the muscles from their insertions, the periosteum was scraped back with a blunt-pointed elevator and all the muscular attachments separated with the same instrument. By this method, and the use of aseptic wax for a few bleeding vessels in the bone, the hemorrhage was reduced to a minimum. The opening through the occipital bone was made with a small oval-pointed, semicircular edged chisel, and enlarged with rongeur forceps to one and one-half inches long by one and one-quarter inches wide. This was very easily done, for the bone was not thicker than thin blotting-paper. The dura mater bulged into the opening and did not pulsate. On pressure with the tip of the finger it felt like a well-inflated bicycle tire. As a measure of certainty I cut a narrow channel across the bone to the left occipital fossa. Here the bone was thicker and the intracranial pressure less. The opening into the dura was made with a knife by cutting down through it, and enlarged with blunt-pointed curved scissors. There was only the smallest quantity of cerebrospinal fluid lost. Before the opening in the dura had been extended one and one-half inches long the brain was forced through, forming a mass half as large as an English walnut. The pressure was so great that I could not palpate the brain within, so I cut the protruding mass away. In an instant more brain was forced out, and this I also cut away. Only one artery from the cut brain surface bled, and this I controlled by touching lightly with a sharp point of a Paquelin cautery. I could then examine the brain with my finger, but could find no hardness which suggested a tumor.

[1] I had the assistance of Drs. Hilt, Ward, Bruce, Rea, Bledsoe, and Mr. Gulledge, a medical student.

During all this time the brain was irrigated with hot sterile salt solution. The portions of the brain removed and the cut surface presented an appearance which I thought at the time indicated an infiltrating lesion of the consistency of the healthy brain. Subsequent examination of the tissue removed showed it to be healthy, only stained here and there with blood—most probably operative hemorrhage. I decided that the growth could not be successfully removed unless I exsected most or all of the right cerebellar lobe, and this I did not think advisable. I purposely refrained from exploring the cerebellum with an aspirator needle or probe, although at one time I had the needle started into the brain tissue. This, however, was probably unfortunate, as it would most likely have revealed and evacuated the cyst. However, I chose to stop the operation, closed the dura, and hoped that the tumor would grow out of the opening of the bone and become more accessible to an operation in the future. The condition of the patient also warned against much further operative interference. With some difficulty the dura was closed over the brain with a continuous silk suture. The scalp wound was united throughout with silkworm-gut and a moist antiseptic dressing applied with moderate pressure.

The patient stood the operation well until toward the last. Hypodermics of strychnine had been given before and during the operation until she had taken fully the twentieth of a grain. As she was put into bed her respirations became very shallow, and in a moment ceased. Her pulse was fairly good and not much above 100 to the minute. I began artificial respiration, which was kept up for fully twenty-five minutes—the pulse remaining about the same—before she breathed; then two or three shallow respirations and a deep one, and an interval of a minute or more, and then shallow respirations again, gradually deepening until the breathing became established. Strychnine was given in one-sixtieth grain doses, internally, during the afternoon and night.

June 16th. Her general condition was good. She wanted breakfast, and a small quantity of food was allowed, which was eaten heartily. During sleep the night before her eyes had been closed, which gratified her mother very much. Her mind was clearer and more natural; the facial paresis was hardly noticeable. The pupils were only slightly dilated, and there was some reaction to light.

The recovery from the operation was uneventful. There was no rise of temperature beyond 99.5°, which occurred on several afternoons. On the eighth day after the operation I removed the dressing and most of the stitches. Union had been perfect. There was, however, a large hernia cerebelli, and I feared the wound would break from the pressure underneath the scalp, but this did not occur. Further examination revealed the fact that the weakness in her left side had greatly diminished; indeed, it was about as strong as her right. As she lay in bed her arms and legs were quite strong and their coarser movements fairly well co-ordinated. In the finer movements the inco-ordination was more marked. Her appetite had grown to be voracious. About this time there began an abnormally rapid growth of the body, which was noticed by everyone who knew her. She could not sit up in bed and would not attempt to raise herself up without something above to hold to with her hands. Two weeks later—about three weeks after the operation—when supported or tied in she could sit in a chair, but would tumble

out in any direction the moment the support was removed. She could hold herself in, however, with her hands, by forcing herself hard against the back of the chair. While she could not stand or walk, she soon learned to crawl, which was done by placing her hands on the floor far apart, as a base of support, while her hips and legs would lie more inactive on the floor; then, in an unsteady, ungraduated manner, she would move her hands forward and drag her hips and lower extremity along. Later she was able to lift herself on her knees, and in this way could get along pretty well. She went up and down the steps and all about the house, and could also sit in a rocking-chair, and, with hands tightly grasping the sides, jump it about the floor.

She was cheerful and happy, and much of her original brightness had returned. The optic neuritis had subsided to some extent, but the eyesight had not improved; indeed, if it had changed at all, it was for the worse. She regained control of the sphincters. The knee-jerks were still totally absent in both legs. Her parents considered her very much improved in every respect except her eyesight.

During the second month after the operation the pressure symptoms became more marked. The paresis of the right facial nerve appeared again, the pupils were dilated as before, and were inactive, and the weakness of the left side was again established.

Her mental condition did not suffer in proportion to the other symptoms. The hernia cerebelli grew constantly, and became half as large as a medium-sized apple; it was also very tense. Headache, vertigo, or vomiting did not return, and she retained control of the sphincters.

A day had been fixed for the second operation, when the following accident occurred. Seated in a large-armed rocking-chair, by some means she pulled it over on her, and fell with her face against the floor, the top of the chair striking the protruding brain. This was August 17th. She screamed and complained for a few moments, and then became unconscious. I saw her in a short time after the fall. She was lying in bed, now and then moving her arms and legs; she could not speak, nor could she be aroused by loud calling; her corneæ were insensitive and the pupils widely dilated. Her breathing was shallow and slow, pulse full, strong, and not rapid, and the hernia cerebelli tense and hard. I decided that the chair in striking the unprotected mass of brain had ruptured a bloodvessel, and that there was a hemorrhage either into the tumor, or into the cerebellar fossa, or perhaps into the fourth ventricle.

An operation was decided on as soon as it was possible to prepare for it.

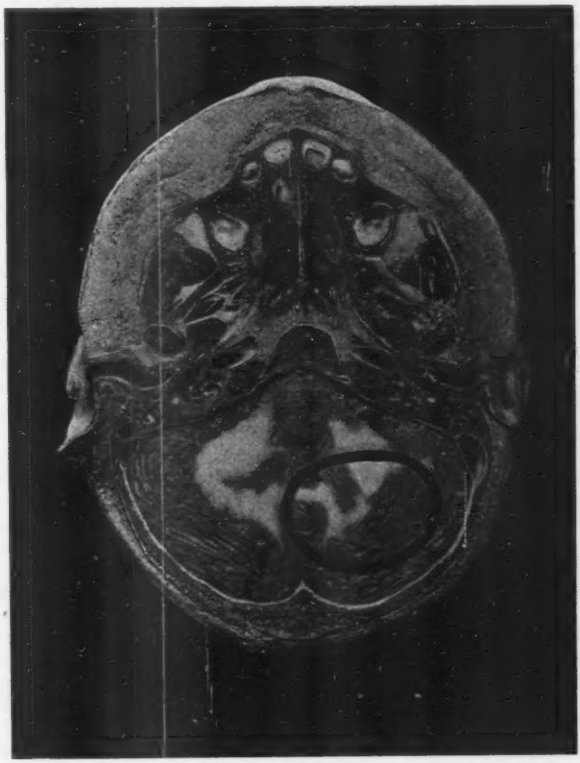
I operated at 11.30 A.M. of the same day, with the assistance of Drs. Love and Rea and Mr. Denny. During the morning strychnine in one-sixtieth grain doses had been given hypodermically. A small quantity of ether was used during the operation.

The incision was made in the line of the old scar; the scalp was thick and healthy, but bled very little. It was easily separated from the mass of brain beneath, over which several bands of dura mater passed.

In examining the protruding mass of cerebellum I found it of a bluish tint, and apparently quite bloodless and easily broken. My finger readily penetrated the hernial tumor, and at once an ounce and a half to two ounces of fresh blood clot was ejected a foot or more away. There was fully as much bloody fluid thrown out at the same time, but

it was lost in the towels and could not be examined. Some fresh blood followed the evacuation of the cyst, the hemorrhage continuing until I lightly packed the cyst cavity with sterile iodoform gauze. As I inserted the gauze I examined the cavity of the cyst; it was smoth in front, but posteriorly seemed to have been made up of irregular masses of compressed brain and membrane.

FIG. 1.



Left. Location of the cyst in Case I., viewed from above. Right.

The cyst had destroyed most of the right lobe, and much of the middle lobe of the cerebellum, and much of the left lobe by pressure. After the cyst cavity had been lightly packed with the gauze there was yet a remarkable emptiness in the cerebellar fossa. I am of the opinion that the direct damage done by the cyst, and the great pressure which it caused, had totally destroyed the functions of the cerebellum. During the operation there was only the very smallest quantity of cerebrospinal fluid lost. The condition of the patient improved from

the moment that the cyst was evacuated. The scalp wound was closed with silkworm-gut sutures, placed farther apart than usual to allow drainage, and a moist antiseptic dressing applied. When put into bed the patient was in a very satisfactory condition. Within two hours she was conscious and able to talk. On the third day the dressing was changed to allow the removal of the gauze packing from the cyst cavity. The dressing was dry, and there had been no loss of cerebro-spinal fluid, nor had there been any further hemorrhage. On August 19th she was in excellent condition. The paresis of the right facial nerve had entirely disappeared; the pupils were about the normal size and reacted to light; and the left side had regained most of its lost strength. There was, however, a marked weakness in her right arm and hand. These members for several days were almost paralyzed to motion.

A rapid operative recovery was made, and all the dressing and stitches were removed by the tenth day after the operation. Her appetite was good from the first, but was never voracious again.

I will not speak further of her condition until the end of the third week after the final operation. At this time the "shock" of the operation had passed off.

Lying in bed she appeared quite natural and healthy and well nourished; her eyes were not so prominent and the nystagmus was gone. She had fair control of her eyes, and could move them in any direction. There was no paresis of the facial nerve. The scalp wound was firm and healthy, and the opening in the occipital bone, instead of presenting a hernia, was concave, notwithstanding the fact that there was no dura mater over this part of the brain; indeed, all the indications of increased intracranial pressure were gone.

At this period her symptoms were the counterpart of the symptoms produced in monkeys when the cerebellum has been removed as a physiological experiment. Station and locomotion were altogther impossible. She could raise herself in bed by grasping your arms with her hands. When she did so, however, she exhibited the most tumultuous disorder of equilibrium—her head swaying and jumping, and an extraordinary unsteadiness pervading all the muscles of her body. When lying down, her legs and arms (with the exception of the weakness in her right arm and hand, which was fast disappearing) were strong and their co-ordination fairly good except for more delicate movements. Soon she learned to crawl again, which was done as before, with her hands placed far apart on the floor, so as to afford a broad base of support, then dragging her hips and legs along. Her hands were moved forward in a jerky, ungraduated manner. She could climb a ladder, going up several rounds, and while her movements were tottering, she appeared to ascend safely. Her knee-jerks had returned, a little livelier than natural and a little more marked in the right leg than in the left. The weakness of the muscles of the trunk, especially of the back, was even more marked than before the operation.

At the time at which this portion of the paper was written, four months after the final operation, the patient was in a most excellent condition. She was well and strong, and growing normally. She walked well, showing very few defects of co-ordination. All the symptoms that were produced by the intracranial growth had disappeared, except that she was blind. After prolonged exercise there was a slight

tremor in the muscles, a little more marked about the head and trunk than elsewhere.

About a year after the final operation she was shown before a medical meeting in an adjoining State; at that time she was in splendid condition in every way. Walked many miles and enjoyed her visit as much as any blind child of her age could possibly have done. Her health continued good for about three years, and at that time symptoms of recurrence appeared, a solid mass growing into and through the opening made at the time of the operation. She was alive in November, 1902, but would not consent to another operation, though her parents very much desired that she should.

CASE II.—*Tumor of the cerebellum accurately located well forward in the right lobe; successfully removed. Apparent operative recovery. Death on the eleventh day from exhaustion, due to diarrhœa.*

History (Dr. Worth Stevenson). Mr. S. E. D., aged twenty-nine years; athlete, amateur base-ball player; occupation, bookkeeper; had always held positions of importance and with entire satisfaction to his employers. Family history negative. No history of lues; had two attacks of gonorrhœa, first several years ago; had not recovered from second attack when present illness began. At twelve years of age he was struck by a stone from a sling above and just behind the right ear. He was knocked down by the blow and the scalp was cut to the bone, but at the time the bone was considered not injured. He continued at school, and nothing was thought of the injury. A large white scar marks the injured spot. An intimate friend gave the information that several years before the present illness began the patient complained of a most peculiar effect which the smallest amount of any stimulant had on him. There is no history of even moderate drinking. He would on going to bed at night hang his head off the side of the bed for relief of a peculiar feeling in the head, but this feeling was not described as pain. He had also suffered from headaches, for many years before his present illness began, which were treated as migraine and considered as the ordinary migrainous type. In December, 1901, while in church at night, he saw the minister double, and was compelled to close one eye to see him naturally. On leaving the church he staggered so badly that he had to be assisted home. His history here is a little indefinite, but it is most probable that he had been staggering before, as an aunt of his told me that one day, while he was yet at business, she saw him staggering to the right and nearly falling off the sidewalk, and that she said to him that people would certainly think him drunk if he continued to stagger so. After he was assisted home he was compelled to take to his bed, which he kept for two weeks. During his stay in bed headache developed, sometimes diffuse, sometimes in occiput, sometimes frontal. At this time severe and obstinate vomiting made its appearance. He did not lose his appetite, and the bowels were natural. At the end of two weeks he had improved to such an extent that he resumed his work; but he was far from well, and remained at work for a few days only, when the headache, vomiting, and staggering returned with greater severity. He was compelled to take to his bed again, from which he was not able to rise without help, except on a few occasions. Later on he could not get out of bed without help. He lost appetite, but this and the frequent vomiting never led to extreme emaciation, though he lost much flesh and strength. It was

noticed during the early part of 1902 that his vision was failing, and equally in both eyes. It was not noticed that there was deafness in either ear. With the onset of the severe symptoms, attacks, epileptic in nature, appeared. At times he had several of these attacks in one day, then one a day, then missing several days, to have several a day again. After these attacks there was some exhaustion and profuse general sweating. During these attacks the following phenomena were observed: Twitching in either leg; turning the eyes to the right; later, right eye did not turn on account of paralysis of the sixth nerve of the right eye. In some attacks the twitching began in the right side of the face, and the mouth would be turned violently to the right.

One striking symptom was the turning of the entire body, especially the head and shoulders, to the right (screwing-in turning). This turning to the right in bed was a most marked symptom, and persisted without intermission during his entire sickness. He was never comfortable lying in any other way, and would always insist on returning to this position when he was persuaded to lie in any other manner.

Inability to walk or stand was an early symptom, and the turning to the right (screwing-in), whether he was out of bed or in bed, was most striking. When held up he leaned to the right, and would have fallen to the right and backward if allowed to do so.

There was paralysis of the sixth nerve of the right eye, but the time this appeared was not definitely known; there was also the slightest paresis of the seventh nerve on the right side. The paresis did not appear to increase after the epileptic attacks, which began in the right side of the face. No electrical examination was made.

There was absolutely no change discoverable in motion or sensation in any portion of the body. When lying down co-ordination was good in all portions of the body. There was no aphasia of any kind, no mental changes, no tendency to joke or make puns, no unusual hilarity; indeed, his mind until toward the last was normal in every way. There was no loss of sphincteric control, and bowels and bladder were voided naturally.

When the patient came under my care (Dr. Stevenson) in June various things had been done for him by various physicians, but availed nothing. I had him take iodide of potash in gradually increasing doses, but his condition did not improve.

History continued (Dr. Hudson). When I first saw Mr. D. he was in bed, with his head and shoulders turned well to the right, the right side of his face touching the bed. When asked to change his position so that I could see his face he very reluctantly did so, saying he was very uncomfortable except when lying on his side and face, and that there was a constant desire to turn a little farther over. He never lay flat upon his face and abdomen. This is the rotation of screwing in the usual right-hand screw, the head of the patient being represented as the head of the screw.

The expression of Mr. D.'s face was a little peculiar, suggesting the faintest shadow of a cynical smile. There was paralysis of the sixth nerve of the right eye, and a faint paresis of the seventh nerve of the right side of the face, visible only when asked to move his face. The tongue was protruded in a straightforward manner and was otherwise normal. There was absolute deafness in the right ear, both to aërial and bone conduction. Cerebration was a little slow, although entirely

normal otherwise. Members of his family and other acquaintances stated that his mind was perfectly natural and in no way changed from what it had been in years.

A careful examination failed to reveal any change in sensation or motion in any part of the body. He could touch the tip of his nose with either forefinger accurately; could touch his knees with the heel of either foot accurately; lying in bed he could lift his legs and feet in any direction, and could control them apparently without any defects. There was, however, just a suggestion of a little awkwardness in picking up a pin or buttoning his shirt; but this awkwardness was not greater than frequently seen in perfectly normal individuals.

For some months before I saw Mr. D. he had been losing his eyesight, and at the time of my examination could with difficulty count fingers; his vision was lost to about the same extent in both eyes. There was double optic neuritis of about the same degree in both eyes.

The most striking symptom in this case was the absolute inability to stand and the inability to sit in a chair unless the patient held himself in very tightly with his hands. When asked to crawl he could do so very readily, placing his hands and knees far apart so as to obtain a broad basis of support.

There was at the time of my examination no vertigo, and vomiting had almost entirely ceased. He complained more or less of headache, at times in the left frontal region, at times through the temples, but more especially in the right cerebellar region. Percussion did not reveal any point of circumscribed tenderness; but deep pressure revealed a marked circumscribed tenderness over the right lateral lobe of the cerebellum, most marked over the region of the tumor. The knee-jerks and ankle clonus were entirely absent.

During my second visit, while examining Mr. D., he notified me that he was about to have one of the epileptiform attacks. It began in the right side of his face, turning it strongly to the right; the attack lasted about thirty seconds. It did not become general, nor did it produce unconsciousness. It passed off quickly and the face was not more paretic than before. The attack was followed by profuse general sweating, but not by a tendency to sleep and not by increased weakness; indeed, the patient's condition, with the exception of profuse sweating, was practically the same as before the attack. There was no nystagmus.

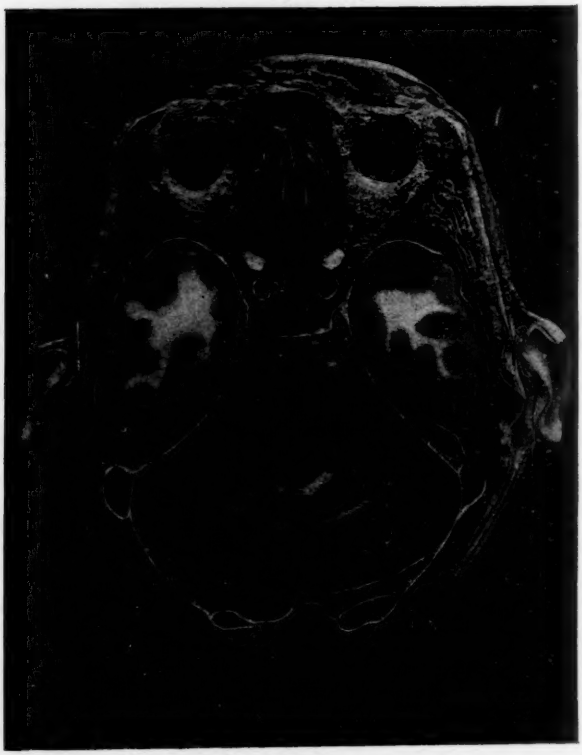
The vomiting, double optic neuritis, headache localized under firm pressure over the right occipital lobe, staggering gait with turning to the right (screwing-in motion), the paralysis of the external rectus of the right eye and the paresis of the right seventh nerve, the deafness in the right ear, the absence of mental failure, and psychical changes indicated that there was a growth in the right cerebellar lobe, most probably situated well forward. An operation was advised, with all of its dangers and uncertainties, and after due deliberation was accepted by the patient's family and demanded by the patient.

The Operation.[1] Ether was the anæsthetic used, and, on account of ether maintaining blood pressure better than chloroform, should be used in preference to chloroform in all operations on the brain. The usual semicircular flap was made and the muscles separated from the

[1] I was assisted by Drs. Hooper, Disharoon, Dean, Stevenson, Floyd, Pate, and Jenkins.

bone with the blunt elevator. A small opening was made through the skull with a chisel and enlarged with rongeur forceps. The dura mater was found very tense, but not so tense as in Case I., and was opened the usual way by cutting through it near the margin of the opening in the bone. The intracranial pressure was much increased and the brain did not pulsate. The brain was explored with the finger, and the tumor found about three-quarters of an inch under the surface

FIG. 2.



Right. Location of the tumor in Case II., viewed from below. Left.

of the brain and in a slightly upward direction. The tumor was of much harder consistency than brain tissue, and was easily made out as a roundish body about the size of a pullet's egg. The finger was pushed behind the tumor and it was very readily enucleated, being fractured when it was pulled against the bony opening in the skull as it was being removed.

After the tumor was removed there was very little hemorrhage, and I explored very carefully and thoroughly with my finger the cavity made by the tumor and by the operative procedure necessary for its removal. Practically the entire right lobe of the cerebellum was destroyed, the tumor having occupied a position well forward in the right lobe of the cerebellum; the long axis of the tumor occupying a vertical position in the cerebellum, the upper pole touching the tentorium cerebelli, the lower pole pointing toward the floor of the cerebellar fossa. The tentorium had evidently been pushed upward to a considerable extent—enough to have pressed considerably upon the right occipital lobe—but we failed to discover any hemianopsia.

As in Case I., the possibility of respiratory failure had been considered; and, not to my surprise, just as the operation was being finished the patient ceased to breathe. Artificial respiration was resorted to, the pulse being very rapid and of very low pressure. It was necessary to continue artificial respiration for more than an hour; in the meantime the patient had come out from the anæsthetic sufficiently to understand what was said to him and to obey instructions. At this time a very curious phenomenon was observed. When artificial respiration was stopped the patient would cease to breathe immediately; but when he was commanded to breathe he would do so, using the voluntary muscles of respiration. At first this voluntary breathing would last about a minute, then breathing would entirely cease. When commanded to breathe again he would do so, the first few breaths being very deep and full; then they would gradually fade away again, each breathing period being longer than the previous one. This process was kept up for fully one hour before normal breathing returned, a person being kept by his side to remind him to breathe when breathing ceased. It appeared that this peculiar breathing process was carried on entirely through the voluntary breathing apparatus, and that the involuntary breathing centre did not assert itself for at least two hours after the breathing first ceased. In other words, the attendants kept up artificial respiration until the anæsthetic passed off sufficiently for the cerebral cortex to resume its functions; then the patient actually continued the artificial respiration on himself through the cerebral cortex and its connections with the intercostal muscles until the natural breathing centre in the medulla could become active again.

In three hours after the operation was performed the patient's condition was entirely satisfactory. His respiration varied from 20 to 30 per minute, and his pulse from 100 to 120 per minute. The paralysis of the sixth, seventh, and eighth nerves had not perceptibly changed, and there was absolutely no change in motion or sensation in any portion of the body by any of the tests used. The knee-jerks remained absent, and never returned again. The other reflexes were also the same as before the operation.

I did not see the patient again until the third day after the operation; at that time he appeared in a remarkably good condition, his temperature normal, and pulse 92 to the minute. He had been able to take egg albumen and beef peptonoid with relish. He spoke hopefully, said he felt very much better than he had felt for months, that his headache was entirely gone, and that his eyesight was very much improved. He had a very persistent inclination to turn over on his right side—screwing-in motion. This was more marked, if possible, than before

the operation. Sensation and motion in legs and arms did not show any defects, and as he lay in bed co-ordination in these members appeared as it did before the operation, there being no discoverable weakness in the arm or leg of either side.

At this time the wound was dressed, and all the stitches and a small gauze drain, which extended to the depth of the wound from which the tumor came, were removed. There had been a slight discharge of bloody fluid, which had so long since ceased that the dressing was dry, and there was no further discharge of fluid when the drain was removed. There was no hernia of the brain, and the entire wound appeared in a perfectly satisfactory condition.

The patient had several times during the few weeks before the operation suffered from attacks of diarrhœa, coming on suddenly and disappearing under treatment within twenty-four hours. On the night of the third day following the operation he had such an attack of a very severe nature, and also vomited at the same time. Calomel and salol

FIG. 3.

Photograph of tumor removed from Case II. Natural size.

were given him by the attending physicians, and when I saw him, at noon on the fourth day, the attack had about disappeared and the patient was in much the same condition as on the previous day, except that he was a little weaker and a little less hopeful, and did not take his nourishment with quite the same relish.

During the fifth day the diarrhœa returned, almost choleriform in nature, and his condition became perceptibly worse. He took nourishment badly and vomited occasionally, at the same time a mild intermission in breathing appearing. The wound was dressed again and the healing appeared perfect. On the eighth day the dysentery was not so bad, but he refused nourishment; his mind was very sluggish; he failed to answer questions; evidently did not understand what was said to him. His arms sweated profusely and were cyanotic, though in the other portions of the body sweating was not marked and the circulation was not changed. There was at this time most marked Cheyne-Stokes respiration, but there were no other signs of compression. Nevertheless, I feared there had been a hemorrhage into the tumor cavity, which had perhaps implicated the fourth ventricle; conse-

quently, I explored the wound, but found no evidence of hemorrhage. There was quite a quantity of cerebrospinal fluid after the exploration, and the breathing very much improved for several hours. The patient's condition did not change until the afternoon of the ninth day, when all of the symptoms grew more unfavorable again, and he died from exhaustion on the eleventh day after the operation. It is very probable that the attacks of diarrhœa before and especially after the operation were due to involvement of the vagus by the tumor and more especially by the trauma of the operation.

No post-mortem examination was allowed.

The tumor was examined by Dr. Simon Flexner and found to be tuberculous.

The localization of tumors of the cerebellum, in the present state of our knowledge, appears to be a very difficult problem. In the hands of the most accurate observers mistakes in localization are about as frequent as successes, and up to the present time there seems to be no symptom or class of symptoms which are to be depended upon as positive in their localizing value.

Some cases of tumors in the lateral lobes have been reported which have produced no symptoms whatsoever, and were only found accidentally at the necropsy. Other cases have presented symptoms which were considered positive of the tumor being located in one lateral lobe, when in fact it was in the other; while other cases presenting all the classical signs of tumors of the cerebellum have proven that no tumor existed in the cerebellum at all, but instead there was found a dilatation of the ventricular system of the brain, more especially of the fourth ventricle, the result of previous meningitis and obliteration of the foramen of Magendie.

The cases reported here have been, perhaps, more than usually favorable for the accurate localization of the tumors. Let us see what symptoms in either case were deciding ones in locating the lobe in which the tumor existed. First, in Case I. there was positive localized tenderness on deep pressure over the tumor. In this case there was paralysis of the external rectus muscle of the eye on the side of the tumor. There was also paresis of the seventh nerve on the side of the tumor. There was also pain in the back of the neck on the same side of the tumor. These were the localizing symptoms in Case I. which led to the decision that the tumor was in the right lobe. There was also considerable loss of strength in the left side of the body, which was consistent with pressure in the right lobe of the cerebellum, pressing upon the pyramidal tract above its decussation. There was also a certain rotation in walking, which was considered of no localizing value.

A procedure at the operation which had never been done before nor since, nor has every been recommended by anyone, so far as I know—that of cutting a channel across to the opposite lobe—was of most positive value, and one which I would recommend in all cases where

there is a question of localization. In this case the bone over the tumor was thinner than the bone over the lobe which did not contain the tumor; and the intracranial pressure was quite perceptibly different over the two lobes, being greater over the lobe containing the tumor.

In Case II. we have a similarity of localizing symptoms: First, the positive localized tenderness on deep pressure; second, paralysis of the external rectus of the eye on the same side as the tumor; third, paresis of the seventh nerve. But, different from Case I., there was absolutely no change from the normal in either side of the patient, either in sensation, motion, or strength. There was, however, one symptom which was considered of great localizing value, viz., absolute deafness, both to aërial and bone conduction, in the ear on the side of the tumor. There was also in Case II. a most decided rotation of the body on its long axis from left to right—the screwing-in turning of the ordinary right-hand screw—but as a localizing symptom this was considered of no value.

In Case II. a channel was not cut across to the opposite lobe, for the reason that the localization of the tumor in the right lobe was reasonably certain.

In Case I. the very slight involvement of the cranial nerve led to the belief that while the tumor was perhaps intramedullary, it was not so far forward as to lie upon the petrous portion of the temporal bone. In Case II., on account of deafness in the right ear and the possible involvement of the vagus nerve, the tumor was considered very probably well forward in the cerebellum; so that when the tumor was not seen after opening the dura mater it was considered proper to explore the cerebellum with the finger in the search of it.

There are some symptoms in the foregoing cases which, studied before and after the operation, are of sufficient importance to be considered somewhat in detail:

The Knee-jerks. When I first saw Case I. the knee-jerks were totally absent, and continued so to the time of the final operation. A very short while after the operation the knee-jerks had reappeared a little more marked than natural and to a greater degree in the right leg than in the left.

The destruction of the cerebellum in this case was, I believe, more extensive than in any other case reported in which an operation had been performed, and yet the knee-jerks promptly returned, and I cannot see what caused their return except the relief of pressure.

In Case II. the knee-jerks were absent for weeks before and had not returned, to any degree, on the third and fourth day after the operation, when the patient presented every appearance of a speedy operative recovery.

In the reports of tumors of the brain, and especially in tumors of the cerebellum, a good deal of stress, heretofore, appears to have been laid upon the existence or non-existence of the knee-jerks; but it is

probable that the presence or absence of the knee-jerk is largely an accidental condition, and is dependent either upon intracranial pressure or upon degeneration of the posterior columns of the spinal cord. The fact that the knee-jerks returned in Case I. after the subtentorial pressure was removed would indicate that their absence was due not to degeneration in the posterior columns, but to pressure; and the fact that the knee-jerks did not return in Case II. after the operation would indicate that their absence was due to posterior column degeneration.

Pain. In estimating the symptoms of highest localizing value in the foregoing cases it is more than probable that greater stress was laid upon the circumscribed tenderness on deep pressure than to any other one symptom, unless it was a total deafness in the right ear in Case II.

Ferrier called attention to deep tenderness many years ago, and thought that it was of great localizing value.

A distinction should be made between superficial tenderness, which is frequently found in the headaches of intracranial tumors, and the tenderness on deep pressure, which was so admirably shown in the two cases here reported. The superficial tenderness, while it may be of considerable localizing value—as, for instance, in the muscles of the neck or below the external occipital protuberance in the lesions of the cerebellum—yet, generally speaking, it is not to be depended upon as an aid to localization, and is dependent upon general intracranial tension.

The deep tenderness and the definitely localized pain is of the highest value for localization, and is of meningeal origin, pointing either to a primary or secondary affection of the dura mater; and, as the foregoing cases prove, the dura mater may be rendered sensitive to deep pressure by a subcortical growth some distance away.

Rotation and Staggering. In Case I. there was staggering in a certain direction, namely, to the left; and just before the patient entirely lost ability to walk there was staggering to the right, but never a constant way of falling; but at no time could any localizing value be attached to these symptoms.

In Case II. there was a most marked rotation to the right—screwing-in turning—and staggering in the same direction. This existed for several months before the operation was performed, but to a more marked degree afterward, and practically when almost the entire right lobe of the cerebellum was destroyed. The rotation to the side of the tumor was in this case certainly due to a destructive lesion, which is in keeping with the accepted opinion on this subject.

It is believed that irritative lesions cause a rotation away from the side of the tumor, and destructive lesions toward the side of the tumor.

The main difficulty, it would appear, arises in deciding whether the lesion is an irritative or a destructive one; and until this problem has

been solved much more dependence must be placed on more positive signs, such as one-sided paralysis of cranial nerves or circumscribed deep tenderness.

In studying the mechanical arrangement of the cerebellum and its bony and membranous envelopes it appears very probable that a tumor growing on the side of the cerebellum might push the brain against the solid bony wall on the opposite side, and produce paralysis on the side opposite to that in which the tumor grows, thus, as it were, producing symptoms by *contre coup*.

In Case I. there was loss of strength on the side of the patient opposite the tumor before the operation, due to pressure on the pyramidal tracts above their decussation; after the operation the weakness disappeared from the opposite side, but there was marked loss of strength in the arm on the side of the body corresponding to the location of the tumor. In Case II. there was no change in either side of the body before or after the operation.

From the standpoint of the surgeon, it is very desirable to know whether the tumor is in the median lobe or in the right or left lobe of the cerebellum; whether the tumor is extramedullary or intramedullary; whether it is situated in the anterior portion of the cerebellar fossa, or in the posterior portion of the cerebellar fossa, or in the petrous part of the posterior fossa; and to clear up these points the following symptoms need to be studied further:

The relation of pain, headache, or tenderness on deep pressure to the location of the tumor in the cerebellar and posterior fossæ, and to extramedullary and intramedullary tumors.

The relation of rotation and staggering to tumors located as specified in the above paragraph.

Hemiparesis and its relation to the side of the cerebellar growth.

Whether or not symptoms on the opposite side to the tumor are ever produced by *contre coup*. If symptoms are produced by *contre coup*, to differentiate these from the symptoms produced by the direct pressure of the tumor.

A careful study of all tumors by the X-ray.

Method of Operating on the Cerebellum. If the operation is to be performed on the right lobe, the skin incision should commence at a point on the superior curved line, half-way between the external occipital protuberance and the mastoid process on the left side of the skull. From this point it should be extended in a semicircular direction to the tip of the mastoid process on the right side, reaching a point about half an inch above the centre of the superior curved line on the side of the skull into which the exploration is to be made. When this flap is fully separated it will allow the exposure of the bone down to the margin of the foramen magnum, and when it is pulled toward the left the centre of the left fossa can be readily reached. By extending

the incision to the tip of the mastoid on the left side the entire occipital region can be laid bare. The flap should be carefully separated from the bone, so as to leave the surface of the bone smooth, and all bleeding stopped by rubbing aseptic wax into the bleeding points. The opening in the bone should be made well below the lateral sinus with a small, semicircular, oval-pointed chisel and enlarged with rongeur forceps. The opening should be as large as the region will safely admit and, if deemed necessary, a narrow channel should be cut across to the centre of the opposite fossa. All bleeding from the cut surface of the bone should be promptly stopped by the use of aseptic wax. After the opening in the bone has been made and the edges carefully smoothed, the dura mater should be examined (if necessary, of both lobes) to see if there is a difference of intracranial pressure. The incision in the dura should be made, as in other operations on the brain, sufficiently far from the cut edge of the bone as to allow the edges of the dura to be sewed together. When the dura is opened, if the tumor is not immediately under the opening the intracranial pressure will generally be so great that a portion of brain will be forced out. If necessary, this should be cut away and all bleeding carefully stopped; then with the forefinger, either with gloves or without, a careful exploration should be made. If the tumor is of harder consistency than the brain it will be felt with the finger. Should the tumor be expected to lie well forward, the finger should be gently pushed for a considerable distance into the brain tissue. If an intramedullary tumor is found, the surgeon must decide as to its size, position forward, and whether or not it is distinct from the brain tissue or has infiltrated it. The condition of such patients is desperate, and when a tumor is found an effort should be made to remove it entire or partly, even to the extent of exsecting a portion of one lateral lobe.

If the tumor is suspected of being in the median lobe, the opening should be made to one side or the other of the occipital sinus, the dura opened here, and the median lobe explored. Should the tumor be found, the opening should be extended across to the other lateral lobe, the occipital sinus ligated, and the dura divided at a point below the lateral sinus. This will allow a slight examination of the upper surface of the cerebellum, depending on the amount of intracranial pressure.

If a cyst is found it should be freely opened, and if deep-lying no effort should be made to remove the cyst wall, but gently pack with sterile iodoform gauze. If the cyst is superficial an effort should be made to remove the wall.

There can be no doubt but that most cases are more safely operated on in two stages. At all events, when there are any indications whatsoever for this necessity, as soon as the bone opening is finished the scalp should be closed over sterile rubber tissue and the operation finished three or four days later.

REVIEWS.

THE TREATMENT OF FRACTURES. By CHAS. LOCKE SCUDDER, M.D., Assistant in Clinical and Operative Surgery, Harvard University Medical School; Surgeon to the Out-patient Department, Massachusetts General Hospital. Third edition, thoroughly revised, with 645 illustrations. Philadelphia and London: W. B. Saunders & Co. 1902.

THE third edition of Dr. Scudder's excellent work opens abruptly with the consideration of fractures of the skull. Here, as throughout the book, he deals at considerable length with features which pertain not alone to the treatment, but which are inseparable from other general considerations. For example, in this chapter he goes rather extensively into the matter of hemorrhages, both intra- and extracranial, along with brain lacerations, compression, exudations, etc., evidently holding that the prognosis and treatment of skull injuries depend rather upon the condition of the soft parts within and without than upon the mere lesion of the bone. Throughout the work also he considers symptoms at length, all of which makes the work much more complete and valuable, but goes a little beyond its announced scope. Differential diagnosis, even, is carefully considered, and he takes pains to emphasize the fact that an unconscious man with a scalp wound and a breath smelling of liquor is not necessarily drunk, but may have an intracranial lesion.

In the treatment of fractures of the jaw he portrays a number of interdental splints, and shows how the less elaborate of them may be constructed by a surgeon who is not trained in the technique of the dentist. He gives an excellent description of the symptoms of fracture of the spine, and even goes to the length of illustrating transverse sections of the cord, showing the effects of hemorrhage and laceration. He takes the ground that in partial lesions operation may be called for, that it is always justified in fractures of the laminæ and spines as well as in all lesions of the cauda equina, whereas in nearly all complete lesions it is contraindicated. He thinks that in these latter cases the expectant method of treatment is best, but advises correction of deformity when present and immobilization of the spine in a plaster jacket.

In discussing treatment of fractured clavicle he has failed to refer to the important demonstration which we owe to the late Dr. Moore, of the relations of the pectoral muscle to the collar-bone, and the advantage which may be taken of these to secure better position of fragments. The same is true of the studies of separation of the upper epiphysis of the humerus, the displacements of which were carefully studied by Moore. The author seems keenly alive to the importance of the so-called carrying function and angle at the elbow, upon which Allis insisted years ago, and recognizes the position of the internal condyle as the key to the

situation. The advantage of confinement in bed with traction in proper direction in the treatment of certain fractures of the humerus is not alluded to. He apparently does not favor wiring a fractured olecranon when the fracture is not open. For Colles' fracture he seems to prefer padded wooden splints to other treatment, and here again he has practically disregarded the advantage of Moore's teaching on this subject.

He goes quite fully into the diagnosis and treatment of fractures of the hip, and wisely warns against prolonged search for crepitus and against all unnecessary movement. He recommends the Thomas splint when the fixation method is thought wise. His directions for treatment of fracture of the thigh are excellent, although he seems to be no friend of anterior suspension. It is rather curious that, although this method originated in the East, its present advocates seem largely confined to the West. But cursory mention is made of fat-embolism on page 322, although it would seem to deserve much more careful consideration. The author recommends operation for fracture of the patella only when it can be done with exceptional judgment and great skill, and not in cases where the separation of fragments is less than an inch. His position in this last regard seems to us ultra-conservative. He has very little to say concerning ambulatory treatment in the body of the book, but devotes a concluding chapter to the subject. He seems to think that plaster furnishes us about the best method for this purpose. There are chapters also on Anatomical Facts Regarding Epiphyses, on Gunshot Fractures, including some interesting illustrations borrowed from recent sources, and on the use of the Röntgen rays, the last being contributed by Dr. Codman.

Finally, while saying very little about plaster splints in the body of the work, he devotes a chapter to the subject at the end, in which he offers suggestions concerning, and illustrations of, moulded and other plaster splints that might well have been introduced into the body of the work. In our own opinion nearly all rigid splints for fractures of the upper extremity can be best made of moulded plaster, and the others might well be thrown away.

The work is most valuable and suggestive throughout, and is more than a treatise on treatment. It is essentially a work on the general subject of fractures, omitting all considerations of surgical pathology. It is lavishly illustrated, averaging more than one illustration to a page, and will make a valuable addition to the library of every one who expects to ever treat cases of this kind. R. P.

INTERNATIONAL CLINICS. Edited by HENRY W. CATTELL, A.M., M.D., Philadelphia, Pa., U. S. A. Twelfth series, 1903, Vol. IV. Pp. 317. Philadelphia: J. B. Lippincott Company, 1903.

THERAPEUTICS is well represented in this volume by Gardiner on a "Sanatory Tent for Tuberculous Patients," who illustrates fully by drawings his idea of a feasible plan whereby they may obtain all the benefits of open-air treatment. Stern offers an elaborate and thorough paper on "Gastric Catarrh," while de Santi takes up in a practical way the "Early Diagnosis and Treatment of Malignant Laryngeal Dis-

eases." Lancereaux sums up the present knowledge of "Gelatin Therapy in the Treatment of Aneurisms." Selected prescriptions for various kinds of diseases and symptoms occupy seven and one-half pages. We would suggest that a search of the formulæ of several dispensaries might have resulted in a more valuable chapter. A posthumous paper by Packard, reporting a "Case of Pernicious Anæmia, with Extensive Pigmentary Changes in the Skin," fully maintains the high reputation for the accurate observation of its lamented author, and the reviewer but voices the general regret that no longer will this brilliant clinician contribute to the alleviation of human suffering and add to sound medical science. Henry, with a pathological report, and practical papers by Flick, Bishop, Bosanquet, and Kelly make the section devoted to Medicine of unusual interest. Of especial mention and commendation is "Scars and Marks of Clinical Interest," by Hall. Chase on the ever-varied subject of "Paranoia;" Spiller, on "Traumatic Brain Lesions in their Relation to Operations." Shewal and Schlaph, on various forms of "Hemiplegia" amply represent Neurology. Surgery is occupied by Fallon, Moynihan, Bodine, Eisendrath, and Leser, offering short papers on various subjects; "Narcosis" being especially considered. Van Harlingen contributes the one paper on "Dermatology," and adds another suggestion for the various phenomena assumed to be hysterical. Shoemaker has given the results of his study of the significance of "Binocular Diplopia." "Biographical Sketches of Eminent Living Physicians" deal with Wood and Keen. Why eminent? The average critic would ask more and denominate them illustrious, for through their labors both medicine and surgery have been amply illumined. Finally, Brown, in his review of the recent and important work on the "Blood in Health and Disease," places us all under obligation, not only from the results of his industry, but as well for the critical spirit in which he has gone over the labors of others. This volume is especially rich in well-selected and illustrating illustrations. In saying that this volume is excellent in excellent company, we only pass a deserved tribute to an energetic and discriminating editor.

R. W. W.

DEVELOPMENT AND EVOLUTION, INCLUDING PSYCHOPHYSICAL EVOLUTION, EVOLUTION BY ORTHOPLASY, AND THE THEORY OF GENETIC MODES. By JAMES MARK BALDWIN, Stewart Professor in Princeton University. London and New York: The Macmillan Company, 1902.

ALTHOUGH the topics discussed in Dr. Baldwin's book are strictly considered not medical in their scope, there are many men in the medical profession to whom such a work will prove of inestimable value. It will, of course, specially appeal to the alienist and neurologist, and to those engaged in working out the many biological problems with which research work in the laboratory is concerned. The lucid and practical manner in which Dr. Baldwin considers his intricate subject will especially commend his work to those who cannot strictly lay claim to be considered among the ranks of the students of evolution. As he says, in his preface, the book is chiefly intended to take up some of the biological problems which come in closest contact with psychological ones, and his

method has been to interpret the important facts in these problems with especial regard to their interrelation with one another. The result is a work of the utmost importance to students of psychology as well as to those engaged in the study of the physical phenomena of nature.

F. R. P.

CLINICAL TREATISES ON THE PATHOLOGY AND THERAPY OF DISORDERS OF METABOLISM AND NUTRITION. By PROF. DR. CARL VON NOORDEN. Authorized American edition. Translated under the Direction of BOARDMAN REED, M.D. New York: E. B. Treat & Co., 1903.

Two small volumes, the first to appear of a promised number of monographs bearing upon this subject, present in Part I. a Discussion on the Indications for Reduction Cures in Cases of Obesity; and, in Part II., the Treatment of Acute Nephritis and Chronic Contracted Kidney. It is quite unnecessary to call attention to the standing of the author, who is one of the greatest living authorities upon these subjects. These monographs, largely the result of Prof. von Noorden's personal experience in practically dealing with these conditions, together with numerous series of experiments, express his personal views.

In the first volume the question of the desirability or necessity of reduction treatment is discussed in a broad way. The author advises its omission in the old and the exercise of great care in its adoption in the young. In the chapter upon Obesity in otherwise healthy persons, the conclusion is reached that reduction, not urgently needed in mild cases, but desirable for external reasons, should be accomplished by the slow methods.

The association of obesity with diseases of the circulatory system, diseases of the kidney, chronic pulmonary disease, chronic articular rheumatism, gout, nervous disorders, diabetes, and pulmonary tuberculosis is next carefully studied. The dissertation is limited to the most salient and important features, while calling attention to those conditions that indicate the reduction of an obesity that does not of itself apparently warrant this therapy.

Throughout Prof. von Noorden is practical and reasons forcibly. He lays stress upon the necessity of relieving or saving the heart, which can frequently only be done by one of the systems of reduction cure. The advantages or disadvantages of particular methods under given circumstances are pointed out.

The second volume, longer than the first, describes the customary therapy in renal disease, and then proceeds to show the fallacies of some of the commonly accepted doctrines of treatment. In the chapter on the Principles of Saving the Kidneys in Renal Diseases the author emphasizes the importance of depending not upon albuminuria as an index of the severity of the disease, but upon the patient's general condition, making acute nephritis under certain circumstances an exception. His clinical observations and experiments establish the fact that much dependence must not be placed upon variations in the output of albumin unless they correspond to changes in the patient's general condition or important symptoms.

Metabolism is discussed in the third chapter. A careful analysis of which end products are excreted with difficulty by the kidneys, and

which are well excreted, is made as a basis for determining those articles of food that should be eliminated from the diet list.

The last half of the book is given over to the principles underlying the dietetic and physical treatment of acute nephritis and contracted kidney. Drugs are concisely dealt with. The desirability of a pure milk diet in acute nephritis is denied. A few things are mentioned which added to milk reduce the ingestion of protein material, at the same time aiding its digestibility.

In the treatment of contracted kidney, the best methods of saving the kidneys and supporting the heart are pointed out. Beverages, meat, condiments, alcohol, allowance of water, and the amount of proteid that should be ingested are discussed. Dark meats, as a class, are judged to be no worse than light meats by the author, whose conclusions are the result of extended observations in practice. Recognizing the value of theoretical experiments, Prof. von Noorden places his reliance, however, upon carefully recorded clinical experience. The book ends with a review of the physical methods of treatment and their value.

H. L. C.

AMERICAN EDITION OF NOTHNAGEL'S PRACTICE.

DISEASES OF THE BRONCHI AND PLEURA; PNEUMONIA. Diseases of the Bronchi. By DR. F. A. HOFFMANN, of Leipzig. Diseases of the Pleura. By DR. O. ROSENBACH, of Berlin. Pneumonia. By DR. F. AUFRECHT, of Magdeburg. Edited, with additions, by JOHN H. MUSSER, M.D., Professor of Clinical Medicine, University of Pennsylvania. Octavo, 1030 pages, illustrated, including 7 full-page colored lithographic plates. Philadelphia and London: W. B. Saunders & Co., 1902.

THE fourth volume of the American edition of Nothnagel's *Practice* is the worthy successor of its predecessors, and in some of its features even shows an improvement over them.

The contents of this volume are divided into four sections; the Anatomy, Physiology, and Pathological Lesions of the Bronchi are discussed by F. A. Hoffmann, who also writes of Emphysema and Atelectasis. Inflammations of the Lungs are discussed by E. Aufrecht, and Diseases of the Pleura by O. Rosenbach. It is needless to say that each section is written in a scientific and thorough manner, and the most recent results of German scientific research incorporated in the text.

The American editor, Dr. Musser, judiciously indicates by notes embodied in the text the points in which his own views differ from those of his Teutonic colleagues. He has also added to the German edition considerable material which will prove of especial value to the American reader. Recognizing the well-known disregard of American and English literature on the part of the Germans, the German bibliography of the different subjects considered in the volume has in each instance been supplemented by a very extensive list of the English and American publications bearing on the subject. Dr. Musser has also incorporated in the text the result of the work done by American clinicians and investigators, which is so invariably ignored by the scientific element of the German medical profession.

The publishers and editors of the American edition of Nothnagel's *Practice* deserve the support and the encouragenent of every member of

the medical profession in America, not only because the books will be invaluable as aids in their work, but because they serve to emphasize the vast amount of practical and scientific work now being done by the physicians of the United States, and in this way tend to elevate the position of the entire profession in this country. The handsome way in which the volumes are got out, and the excellent quality of the illustrations which accompany them, add greatly to the value of the series.

F. R. P.

THE PRACTICAL TREATMENT OF STAMMERING AND STUTTERING. By G. B. LEWIS, M.D.; and A TREATISE ON THE CULTIVATION OF THE VOICE. By G. A. HYNSON, M.D. Illustrated. Detroit: George Andrew Lewis, 1902.

THE authors state in the preface that this book is the result of the experience of two teachers who are specialists in their respective departments, and whose aim in writing has been to aid those having gross defects of speech and those who seek a higher cultivation of the voice.

The book is written in two parts. The first part treats of stammering, and covers 166 pages. While it contains good advice to the stammerer, one feels that it might have been said better in fewer words. Indeed, there seems to have been throughout on the part of the authors an effort to make a big book, and this has led to repetitions and the introduction of useless material. Several pages, for instance, are devoted to the differential diagnosis between stammering and stuttering, whereas the fact is, as they themselves finally admit, that they are merely different stages of the same affection.

Moreover, not many authorities will agree with their claim that stammering is primarily a *mental* disease. Any physical obstruction to normal speech may be the *primary* cause of stammering, and it frequently becomes *secondarily* a mental habit.

In one place it is stated that the stammerer in everything save speech is an average person, and in another place that "his mental and moral nature is dwarfed by his affliction." This would seem to be a contradiction.

"A lisp," they say, "is not due to improper structure of the organs, but to their misuse." Who of us has not seen lisps due directly to structural deformities of the superior alveolar arch and irregular teeth? Indeed, "improper structure of the organs" is probably the most frequent primary cause of lisping. Again, the authors claim to have examined 10,000 cases of stammering, and to have found only one among them having any organic defect. The only possible explanation of this statement is that the examinations have lacked thoroughness, or that they were made by someone unable to recognize organic defects.

The second part treats of the cultivation of the voice. Unfortunately, there is no science of voice culture, and every teacher has a method of his own. Any method is better than no method, and, therefore, all teachers may do some good. Not much good is accomplished, however, by the writing of books on the subject, and only those teachers who have proven the correctness of their theories should go into print.

In the volume before us the vowels I and U are classed as elementary sounds, whereas an analysis of them will show the former to be com-

posed of two sounds, Ah and E, and the latter to be the equivalent of E and OO. In the section on Breathing the authors refer to the intercostals as the chief inspiratory muscles, and the great muscles running from the thorax to the shoulders are entirely ignored. The intercostals are rather more expiratory in their function than they are inspiratory.

Speakingwhile walking up hill is recommended to improve the voice. While this exercise doubtless strengthens respiration, it can but impair the voice, because it opposes the normal action of the vocal muscles when speaking without walking up hill. It is safe to say that no other physical exercise is admissible while practising voice culture.

Notwithstanding its flaws, the book doubtless has some practical value for those who are so unfortunate as to stammer, and for those who would improve their vocal utterance, and yet even these must be very limited, because both classes, as the authors have stated, require the living teacher.

M. S. S.

A MANUAL OF MEDICINE. Edited by W. H. ALLCHIN. Vol. IV., Diseases of the Respiratory and of the Circulatory Systems. New York and London: The Macmillan Company, 1902.

WHEN confronted with a problem in pulmonary or cardiovascular disease one naturally turns for information to the English writers, who have contributed their full share to our stock of clinical and therapeutic knowledge in this important field. It is in the management of chronic cases of this kind particularly that a wide practical experience on the physician's part tells more, perhaps, than a minute acquaintaince with pathological changes. Nevertheless, the plan adopted in the present manual of disposing of the morbid anatomy in a separate section before discussing the symptomatology, diagnosis, and treatment of the individual diseases, while convenient, tends too much to dissociate the study of morbid changes from that of the corresponding clinical manifestations. On the other hand, the introductory physiological epitomes are excellent, containing, as they do in a compact form, the essential facts for a proper understanding of the subject. In speaking of cutaneous respiration the author advances a novel theory in regard to the cause of death after extensive burns. "It cannot be attributed to the arrest of the functions of the skin. The success which follows the treatment of patients suffering from burns with morphine and single aseptic dressing suggests that shock of the nervous system is the primary cause of death in fatal cases. The concentration of the blood from the loss of lymph is a secondary cause." If this theory is correct, the time-honored story of the pathetic death of the gilded boy-angels in the mediæval papal procession, that has done duty so long as a classical example of the fatal effects of abolishing the cutaneous function, must go the way of other exploded myths. The description of objective phenomena of disease, especially of the methods of physical examination—in short, the subject of physical diagnosis—leaves much to be desired from the teacher's and student's viewpoint. We note the absence of several questions that deserve at least a mention, whether commendatory or otherwise; and this omission is the more conspicuous as some of the very newest methods of examination, such as radioscopy, for example, receive due attention. The paragraph on the latter is too

dogmatic for such an untried method and much too optimistic in the light of what has been accomplished thus far. One of the most difficult tasks in physical diagnosis is the determination of the areas of cardiac dulness. The various text-books agree in nothing so well as in the obscurity of their language in describing this important procedure, and the present work is no exception in this respect. Thus a careful perusal of the paragraph describing the limits of deep cardiac dulness leaves the reader with an imperfect idea of the author's views in regard to the outline of the area in health. But these defects are not irremediable. The chief value of the book is its presentation of the clinical aspect of medicine. Such important subjects as the prognosis and management of heart cases and of chronic pulmonary disorders, and the treatment of pulmonary tuberculosis are presented in the very best style. The authors hold conservative views on the subject of treatment; they see little to hope from the perennial search for the specific or the promises of serum or antitoxin therapy in pneumonia and tuberculosis. Hygienic control, as against drug-giving and artificial medication, is the stand they take. The disciplinary value of sanatorium treatment is aptly expressed in the statement that it supplies what the patient lacks at home, "the constant encouragement to follow a life of physiological righteousness."

R. M. G.

AN EPITOME OF PHYSIOLOGY FOR STUDENTS AND PRACTITIONERS OF MEDICINE. By THEODORE C. GUENTHER, M.D., of the Norwegian Hospital, Brooklyn, and AUGUSTUS E. GUENTHER, B.S., formerly Assistant in Physiology in the University of Michigan, Ann Arbor. In one 12mo. volume of 250 pages, with 57 engravings. Philadelphia and New York: Lea Brothers & Co., 1903.

THE defects of a quiz-compend are more likely to be sins of commission than of omission, paradoxical as it may sound; for a student's manual, to be valuable, should be not a mere condensation of the entire subject into as small a compass as possible, but a thorough presentation of the elementary and salient points, not necessarily expressed in short primer sentences—not a short-cut to knowledge and an easy road to graduation, but rather the first stepping-stone in the student's ascent to the broader field of independent study and laboratory research. The authors appear to have conceived their work in something of this spirit, and produced a type which, fortunately, is supplanting the older representatives of the class, often little more than a collection of questions and answers, either in form or in effect, with a lamentable dearth of reasoning and explanation. The lists of questions found at the end of each article are intended evidently as a summary of the subject; and, as the answers are left to be supplied by the student, the result is a wholesome test of concentration and mental assimilation. The text, comprising some two hundred and fifty pages and illustrated by a number of engravings and diagrams, is as commendable in regard to diction as the type is acceptable to the eye, which is no small consideration; nor are the pages defaced by an undue number of heavy-faced headlines, although the italics have perhaps been supplied with a somewhat too lavish hand.

R. M. G.

THE PRACTICAL MEDICINE SERIES OF YEAR BOOKS. Vol. IX., Physiology, Pathology, Bacteriology, Anatomy. Pathology, edited by W. A. EVANS, M.S., M.D. Bacteriology, edited by ADOLPH GEHRMAN, M.D. Chicago: The Year Book Publishers, August, 1902.

THIS volume of the *Year Book* includes reviews on physiology, pathology, bacteriology, hygiene, and anatomy. The book numbers a little over 200 pages. The subject of physiology is entirely devoted to a short review of some of the more recent work on antitoxins, precipitins, agglutinins, lysins, and cytotoxins, and is arranged rather as a general exposition of facts underlying the question of immunity than as a summary of the year's work in this department of research. Many of the references are incomplete, only the name of the journal and the year being given, and again certain investigators' work is quoted without any reference. The section on Pathology is the longest one in the volume. It is arranged as a series of short reviews, the separate articles being grouped as nearly as possible under the headings of General Pathology, Special Pathology, and Laboratory Diagnosis. The same general scheme of arrangement applies to the section on Bacteriology, but since the chapters on Hygiene and Anatomy together cover only fifteen pages, no subdivisions are made in these two subjects. It is greatly to be regretted that so little foreign literature is reviewed and that most of the references are taken from those American and English journals which are most familiar to the average medical man. The reviews themselves, however, are clear and concise. The subject-matter is well indexed, but unfortunately there is no author's index. W. T. L.

PROGRESSIVE MEDICINE. A Quarterly Digest of Advances, Discoveries, and Improvements in the Medical and Surgical Sciences. Edited by HOBART AMORY HARE, M.D., assisted by H. R. M. LANDIS, M.D. Vol. II. June, 1903. Philadelphia and New York: Lea Brothers & Co.

THIS volume of *Progressive Medicine* is one of the most satisfactory, in our opinion, which has been issued in this invaluable work. The first portion deals with abdominal surgery, including hernia, and contains generous abstracts of all the best recent articles, with well-directed comment by the editor, William B. Coley.

The second portion deals with the most recent gynecological literature, and is excellently prepared by John G. Clark. The medical portion of the book considers diseases of the blood and ductless glands, the hemorrhagic diseases, and metabolic diseases. This section is under the able editorship of Alfred Stengel.

Edward Jackson presents a critical review of recent ophthalmological literature in the latter portion of the volume. The work contains a mass of interesting material, both for the specialist and for the general practitioner, and is prepared by men particularly well suited to the task. As a piece of book-making it differs in nowise from its predecessors. There are many handsome illustrations, which add greatly to its value.

J. H. G.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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A New Hypnotic of Apparent Value.—In March Fischer and v. Mehring published a communication concerning a variety of new synthetic products with hypnotic action. They were all derivatives of urea, and of these diæthylmalonylurea—"Veronal"—was especially recommended. V. Mehring has convinced himself of the efficacy and harmlessness of this drug in human beings. Poly (*Münch. med. Wochenschrift*, 1903, l., 856) in Leube's clinic has tested this preparation in fifty-two patients suffering from insomnia dependent upon a variety of different conditions, with extremely favorable results. In the majority of instances sleep came on in from half an hour to an hour and a half after the administration of the drug. No unpleasant results were observed. The urine was always free from albumin, sugar, or hæmoglobin. In several cases there was a feeling of lassitude on the following morning, even after doses as small as 0.5 (gr. viiss). The drug can also be administered in rectal suppositories. Poly believes that veronal is an important addition to the pharmacopœa.

Lilienfeld (*Berliner klin. Wochenschrift*, 1903, xl., 474) also reports most favorably upon this preparation. He found that doses of 0.5 (gr. viiss) were sufficient to produce from seven to nine hours' sleep, though in cases of feeble women with not very obstinate insomnia a dose of 0.3 (gr. iv to v) was sufficient. The drug is soluble in 12 parts of boiling water and in about 145 parts of water at 20° F., and forms easily soluble alkaline salts. It has a slightly bitter taste. Veronal may be given easily in warm tea or milk. Taken in this manner Lilienfeld has found that it produces sleep often in as short a time as a quarter of an hour. He has found no bad results beyond a slight tired feeling and drowsiness on the following day after doses of 1 gramme (gr. xv) and above. In one hysterical patient an exanthema similar

to that sometimes observed after antipyrin appeared after each dose. No other ill effects, however, were noticed. His observations lead him to believe that the action of veronal is more reliable and stronger than that of any other hypnotic now in use, while it has the great advantage of being cheaper than any of these preparations excepting chloral.

The Pathology of Asthma.—BRODIE and DIXON (*Transactions of the Pathological Society of London*, vol. liv., part i., 1903) believe, from experimental investigations which they have carried on, that, of the four theories advanced to explain the symptoms of an acute attack of asthma, the one which attributes it to a spasm of the bronchial muscles is the correct one. The other theories are as follows: That it is caused by a swelling of the bronchial mucous membrane—fluctionary hyperæmia (Traube), vasomotor turgescence (Weber), diffuse hyperæmic swelling (Clark); that in many cases it is a special form of inflammation of the bronchioles, bronchiolitis exudativa (Curschmann); that it is due to a reflex spasm of the inspiratory muscles, especially the diaphragm.

In their experiments the method of determining the state of contraction of the bronchioles was by recording the volume of air entering and leaving the lung during each respiratory act. This was effected by exposing one lung of an animal—usually the dog—by removing several ribs and then isolating one lobe—generally the right lower—and enclosing it in an oncometer. Aëration was kept up by artificial respiration. The changes in the volume of the enclosed lobe were measured by connecting the oncometer with a bellows recorder.

Their innervation experiments confirmed what had already been known, namely, that the motor nerve of the bronchial muscles is the vagus. Stimulation of the vagus caused a marked diminution in the volume of air entering and leaving the lobe, owing to contraction of the bronchial muscles. They made the interesting observation that the vagus also contains bronchodilator fibres. They first caused a tonus of the muscle fibres by administering muscarine or pilocarpine, and then stimulated the vagus, and there resulted a marked increase in the volume of the lobe, which they interpreted as being due to stimulation of the bronchodilator fibres. They therefore conclude that the bronchial muscles are innervated by two sets of fibres, a constrictor and a dilator set, both of which run in the vagus.

They found that the giving of an anæsthetic seriously interfered with their experiments; so they partially anæsthetized their animals (dogs, cats, and rabbits), and then destroyed the brain and medulla, waiting three or four hours for the effect of the anæsthetics to wear off before commencing their experiments.

While the destruction of the brain and medulla seriously interferes with the study of the effects of reflex stimulation, they have recorded slight bronchial constriction on excitation of the central end of the vagus divided in the neck, and similarly of the superior laryngeal. They obtained no reflex constriction by excitation of a sensory cutaneous nerve, nor by excitation of the stomach or intestines. The most important constrictor reflex of all was obtained by stimulation of the nasal mucous membrane, particularly the posterior and upper part of the nasal septum.

Of drugs, muscarine, pilocarpine, physostigmine, and digitaline produce marked bronchial constriction. Atropine, hyoscyamine, and hyoscine paralyze the vagal endings and cause bronchial dilatation if constriction be previously present. Lobelia causes very marked dilatation, the effect of morphia being less marked. Carbonic acid gas causes marked bronchial constriction.

They then proceed to discuss the practical bearing of these experiments on the etiology of asthma. They dismiss with a few words the other theories as being inadequate. In favor of the view that asthma is due to a spasm of the bronchial muscles is the suddden onset and rapid disappearance of an attack exactly corresponding with what is known to be the common course of a prolonged contraction of involuntary muscle. Moreover, a perfectly typical attack of asthma can be induced in an animal by a small dose of muscarine. There is the same distended thorax, dyspnœa, and sibilant râles. Further, such an attack can be almost instantaneously cut short by the injection of atropine. This would not be the case if it were due to a turgescence of the mucous membrane or to an exudation. The fact that ether and chloroform help to relieve an attack and that they also interfere with the bronchial constrictor experiments point strongly in favor of the constrictor theory. The bronchial dilator action of atropine, morphine, and lobelia points in the same direction.

The writers think that their theory of bronchial constriction amply explains the overdistention of the lungs in an acute attack. The power to deflate the lungs is much less than the power to inflate them, and consequently the overdistention results. Accepting the bronchial constrictor theory as the writers do, they proceed to discuss how the constriction of the muscles is produced. Is it peripheral, central, or reflex? They believe that it is due to central irritation of the vagus in the medulla, but that this is brought about by reflex stimulation. They argue this from the fact that an attack of asthma is likely to be induced by eating a heavy meal. The main source of reflex irritation, however, is the nasal mucous membrane. This was shown in their experiments, and it is amply illustrated by clinical experience.

The Specificity and Practical Value of the Albumin-precipitating Sera.—As is well known, Wassermann, in 1900, described a method for recognizing the albumin of human beings and of various animals depending upon a specific reaction. This method, which he calls the "biological procedure," depends upon the fact that after repeated injections of blood serum of one animal into another there develops in the blood of the second animal a specific antibody, which causes a precipitation of the albumin of the serum of the first animal.

Wassermann's original communication was followed by many researches and a considerable number of publications; and the method has been used for various practical purposes, as, for instance, the recognition of different varieties of meats, the determination of the origin of bits of bone and of blood stains, as well as the recognition of the character of the milk from which a given cheese has been made.

Some observers have, however, doubted the specificity of the method.

Wassermann and Schütze (*Deutsche med. Wochenschrift*, 1903, xxix., 192) refer to the fact, which has been clearly demonstrated by the work of Ehrlich and his school, that when in an attempt to elicit an antibody an animal is inoculated with the serum of another, there develop specific antibodies for all the elements of the injected serum which find in the economy of the animal into which the serum is injected chemical groups which have for them a specific affinity. If we immunize, for instance, against two bodies, *a* and *b*, there is a sharp specificity, which is shown in the fact that the serum of the *a* animal never has the least influence on the *b* body unless there happen to exist in the organism which is being immunized certain chemical groups capable of binding the bodies *a* and *b* in common. Should such groups exist in the blood of the animal into which the serum is injected, then of course the antibodies will act against both *a* and *b*, and the extent of this mutual action will depend upon the number of the groups which bind the two bodies in common. Suppose, for instance, that in the animal being immunized all the binding groups have an equal affinity for the bodies *a* and *b* in common; then the immune serum will act with equal strength upon the two bodies. But if there are only relatively few such groups, then the undiluted serum will act upon both bodies, while the serum which is diluted will influence only one of these substances, namely, that with which the immunizing injections are made, inasmuch as in the dilution the groups possessing a common affinity for both *a* and *b* are present in too small quantity to have an appreciable action upon the second body. In accordance with these conditions, which have been demonstrated by Ehrlich and Morgenroth and Wassermann for the hæmolysins and agglutinins as well, it has been shown that the closer two species of animal are related one to another the more similar is the finer structure of their albumin, and the greater the number of antigroups possessed by them in common. Thus, the serum of a rabbit which has been treated with hens' albumin will cause a precipitation of pigeons' albumin as well, and in the same manner the albumin of the ape may be in part thrown down by a precipitin resulting from the injection of human albumin, and the converse. The same is true with the horse and the ass, the ox and the sheep. It has further been shown by Bordet that the best results are to be obtained when the immunized animal is selected from a species as far removed as possible from that of the animal whose serum is introduced. These facts explain the doubts expressed by some observers as to the specificity of these methods.

Wassermann and Schütze have devoted themselves particularly to the development of a procedure which may be relied upon for the recognition of human albumin. Such a procedure they believe that they have been able to satisfactorily outline. They insist, however, upon the fact that in the carrying out of these "biological methods" of precipitation the utmost care must be exercised; that they can only be applied according to definite rules by observers trained in laboratory methods. For the development of a precipitin for human albumin they advise the inoculation of rabbits, and enter carefully into the steps which should be taken in this procedure.

They insist that this method is not one which permits the diagnosis of the products of special organs. It is, however, a method which allows of a definite diagnosis as to the *species of animal* from which certain forms of albumin,

for instance, casein or serum albumin, come. It is a *species reaction*, and the specific precipitating serum reacts with every substance which contains precipitable albumin from that species of animal. It reacts, therefore, as well with solutions made from bits of bone as with other albumin-containing fluids.

[There can be little doubt that, properly controlled, Wassermann's "biological method" is destined to become of the greatest medico-legal importance. It should give us a means of recognizing the character of blood stains of much greater delicacy than any which we have heretofore possessed. —W. S. T.]

SURGERY.

UNDER THE CHARGE OF

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A Contribution to the Pathology of Intermittent Hydronephrosis; the Renal Pelvis and Ureters of the Newborn.—BAZY (*Revue de Chir.*, January 10, 1903), after reviewing the subject in detail, states in conclusion: Hydronephrosis, and especially the intermittent form, has its origin in the congenital position of the renal pelvis and the accessibility of the ureter. The maximum of the congenital conditions which constituted the hydronephrosis were realized by a large renal pelvis, of horizontal type, rather angled or horn-shaped, very rarely a true position, and that is in accordance with the rarity of intermittent hydronephrosis. The accessory conditions to the production of this hydronephrosis are the narrowing, twisting, and torsion of the superior extremity of the ureter. This hydronephrosis may be the result of a movable kidney. But the position and the mobility of the kidney appear more often to be consecutive to the hydronephrosis. The production of the hydronephrosis is favored by the possible stagnation of a small quantity of urine in a congenitally large renal pelvis, congenitally situated so as to permit this stagnation, and as a result the stagnation occurs under the influence of very small cause. This cause, to repeat, terminates by causing a greater and greater stagnation until one day, when the kidney, having also increased in volume and in weight, may fall, leaving also a new condition of stagnation. At the same time this position created the crisis of the intermittent hydronephrosis. The torsions and bendings, the result of the position, or created or augmented by it, may be fixed and rendered definite by the formation of adhesions or by a parietal sclerosis united to an irritative process, that perhaps may have been determined by an atten-

uated infection or perhaps by a simple aseptic irritation. The intermittent hydronephrosis may become permanent either at the first onset or after repeated attacks. This permanent definite state may be caused by the adhesions retaining the sac and the ureter and obstructing the evacuation of a part of the pelvis of the kidney, because these adhesions have completely effaced the calibre or the lumen of the urethral conduit in a point of its course or, above all, in the region of the entrance of the ureter into the pelvis of the kidney.

Splenopexy for Wandering Spleen.—HALL (*Annals of Surgery*, April, 1903) states that a review of the literature shows only eight reported cases of operation for this rare condition, to which he adds one of his own. The patient, a married woman, aged thirty years, presented the typical symptoms of an enlarged floating spleen, and operation was decided upon for its relief. An incision four inches in length was made at the outer border of the left rectus abdominis, through which the spleen was delivered. It was seven and a half inches long and three and a half inches wide at its centre, and except for size was to all appearances normal. In order to fix the organ in its proper position the main body of the spleen was replaced in the abdomen, after rendering the parietal peritoneum raw in the splenic fossa in order to excite adhesions; then, while the lower pole was held in the wound, the edges of the peritoneum were drawn tight by a purse-string suture until they closely gripped the narrow isthmus in the notch. The abdominal aponeurosis was next sutured in a similar manner until it grasped the isthmus in the notch sufficiently tight to produce marked congestion of the now isolated lower pole. The left rectus muscle was next drawn outward somewhat, so as to overlap the projecting pole of the spleen as much as possible, and then the skin incision was sutured. The patient made an uninterrupted and complete recovery. The author states that the means that have previously been used for the relief of this condition are the excitation of adhesions by tamponade, the formation of a pocket in the parietal peritoneum in which the lower end of the spleen is placed, and the use of sutures.

The Treatment of Fractures.—BORCHARD (*Centralblatt f. Chir.*, 1903, No. 5) states that his method of treatment consists briefly in immediate massage, followed by the support of an appropriate splint retained by bandage. The fragments should be retained in exact apposition as soon as the initial swelling has subsided and until there is good consolidation, which is usually present at the end of twenty-six days. Massage should then again be undertaken, and should be followed by a careful use of the injured part. The advantages of this method of treatment are the avoidance of stiffness of the joints, atrophy of the muscles, and œdema, which often follows subsequently to the use of the limb.

The Avoidance of Ventral Hernia after Laparotomy.—WOLFF (*Centralblatt f. Chir.*, 1902, No. 50) states that he has tried all methods of suturing and used all of the different suture materials, and yet in some cases, despite every precaution, a hernia has resulted. A careful analysis of these cases shows that hernia has only followed in those patients who have had meteor-

ism soon after the operation. The explanation of the appearance of the hernia is that through the pressure of the distended intestine the stitches are mechanically sprung apart. As a rule, the skin suture remains intact, even though the others have pulled out. This is the true explanation of the cause of hernia shortly after operation; the kind of stitch or suture material that is used is absolutely immaterial, and it becomes essential to determine just how meteorism may be avoided. Meteorism and ventral hernia stand in the relation of cause and effect. The author states that he makes it a rule to completely close only those wounds where a rapid and uneventful course of healing is to be expected. In those cases where some slight discharge is to be expected it is best to provide for drainage by a small strip of iodoform gauze, which will tend to prevent meteorism. A two years' experience has shown that when this method of wound treatment is followed the unfortunate sequel of ventral hernia is much less frequent than it formerly was.

Accidental Wound of the Bladder, in the Course of a Radical Cure for Hernia.—VERHOLF (*Annales de la Soc. Belge de Chir.*, February and March 1903) states that a cystocele may be found either to the right or to the left when it accompanies an inguinal hernia, in contradistinction to the case in a crural hernia. Jaboulay has stated that a cystocele has never been found except on the right side, but in one of the author's cases it accompanied a left-sided crural hernia. One should remember, in operating, that in every case of hernia there is the chance of a cystocele being present. In order to recognize the presence of the bladder several methods have been suggested: the introduction through the urethra of a curved metal sound with its point in the cystocele, or the injection of liquid, plain or colored. The introduction of this sound may be valueless, as in one of the author's cases, where the space between the bladder proper and the diverticulated portion may be so small as not to permit the passage of the sound. Injection of a liquid is, as as a rule, a more useful proceeding, but it may fail by reason of the liquid remaining in the dependent portions of the bladder, and so not rising sufficiently to enter the opening into the cystocele. The treatment of the bladder wounds should depend on the situation of the wound and the condition of the urine. If the wound be aseptic and absolutely extraperitoneal, no suture is required and its closure does not prolong nor unduly complicate the result of the operation. If, on the other hand, the urine is infected, ample provision should be made for drainage and the easy evacuation of the bladder contents. If, on the other hand, the wound be intraperitoneal, it should be sutured and provision made for drainage.

A Case of Cyst of the Pancreas, with Remarks on the Pathology and Surgical Treatment.—CUMSTON (*Jour. de Chir. et Annales de la Soc. Belge de Chir.*, January and February, 1903), after reporting a case in which drainage was followed by complete recovery, and considering in detail the symptomatology and pathology of this interesting condition, states that the treatment is exclusively surgical, and the operator has two methods from which he may choose—either incision followed by drainage, or extirpation. The choice of the position of the incision should entirely depend upon the situation of the tumor, but in most reported cases the abdomen was opened in the

median line, more rarely over the most prominent portion of the tumor. If after the separation of the gastrocolic ligament and the peritoneal covering of the cyst one finds that the tumor is either free or its adhesions may be easily separated, total extirpation is evidently the operation which is indicated. If the contrary is found, then incision followed by drainage must be done. After the cyst has been isolated it should be fixed by sutures to either the abdominal wall or the parietal peritoneum. The cyst should be carefully walled off from the peritoneal cavity by pads while it is being sutured. It is advisable to suture the parietal peritoneum to the peritoneum covering the cyst, and after opening the latter it should be sutured to the borders of the skin. After the cyst has been opened and its cavity thoroughly irrigated with sterile salt solution a gauze drain should be inserted. Some surgeons perform this operation in two sittings, but this is not necessary. At the present time the end result of the surgical treatment of cysts of the pancreas is not clearly known. It is evident that in those cases where it is possible to do a total extirpation the chances are against a recurrence, but it should be remembered that there is always the possibility of a cyst developing at some later date in a portion of the pancreas which has undergone cystic degeneration, but which at the moment has not been perceived. In those cases where the cyst is drained there is theoretically a greater chance of recurrence, and there may remain a fistula, which may give rise to various complications. As a rule, however, the secretion from the cyst gradually diminishes and the fistula eventually closes, but in one case reported by Gould the fistula persisted during three years, and in that reported by Gravemann, when seen a year after the operation, the fistula was still open and showed no tendency to close.

THERAPEUTICS.

UNDER THE CHARGE OF

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Iron and Arsenic in Hemorrhage.—DR. E. P. BAUMANN has made a series of researches in dogs, withdrawing a quarter of the volume of blood from the body, and has made subsequent examinations of specific gravity, rate of coagulation, number of red cells, number of white cells, weight of solids, ash, and proteids, under therapeutic administration of Blaud's pills, iron albuminate, and arsenic. Four animals were kept as controls. At the end of a week the blood was re-examined, and the condition was compared to that of the blood of the dogs to whom no iron was given. When an

inorganic iron was given the loss of hæmoglobin was quickly made up, and even increased above its original quantity. With the albuminates similar results were obtained, but none were less striking. Arsenic alone gave little effect, while a combination of iron and arsenic gave the best results as far as the plasma, solids, and the corpuscles were concerned, but there was less new formation of hæmoglobin.—*Journal of Physiology*, 1903, vol. xxix. p. 18.

On a Poisonous Serum to the Heart.—Dr. Luigi Ferranini has obtained a cardiotoxic serum from guinea-pigs and rabbits. He injects into guinea-pigs first an emulsion of frogs' hearts, and into the rabbits an emulsion of toads' hearts. The heart is taken under antiseptic precautions from the living animal, and immediately transferred to sterile physiological salt solution, in which it is washed and finally ground up in a mortar with a cubic centimetre of the solution. As soon as it is prepared it is then injected subcutaneously into the peritoneum of the animal. For guinea-pigs he has injected emulsions from one frog's heart every second day. In others the emulsion was from two frogs' hearts every four days. Rabbits were injected every three days with the emulsion of a single toad's heart, or every six days with the emulsion of two toads' hearts. In all each animal received an emulsion of from sixteen to twenty hearts. The animals were then permitted to leave the cage, the guinea-pigs four days and the rabbits six days after the last injection. In general the guinea-pigs stood the injections better than the rabbits, and the intraperitoneal injections were taken better than the subcutaneous ones. The animals lost weight from the beginning from one-quarter to one-third of their body-weight. Of the rabbits at least one-half died during the treatment, paralysis of the hind extremities appearing twenty-four to forty-eight hours before death. The serum of the treated animals was obtained from the jugular vein, and was then injected into frogs or toads, and the effects on the heart contractions studied. In both instances it was demonstrated that a cardiotoxic serum had been developed, the action of which could be demonstrated with great precision. This is a preliminary communication only; the author promises further observations.—*Centralblatt für innere Medicin*, 1903, No. 15, p. 369.

The Serum Treatment of Basedow's Disease.—Dr. O. Lanz reports on the use of the secretion of thyroid in the treatment of exophthalmic goiter. Cachexia strumipriva has shown that there are certainly in the body of men and animals certain classes of poisons, which are either neutralized or modified by the normal secretion of the thyroid, which poisons by the removal of the thyroid become operative in some way or another. He grinds the thyroid and makes an emulsion of it with milk, with which the patients are fed. In 6 cases there was an improvement and diminution of the tumor and lessening of the tachycardia and a recession of the exophthalmos. The patients took on weight, which, it was demonstrated, was not due to the increased amount of milk that was being taken.—*Münchener medicinische Wochenschrift*, 1903, No. 50, p. 146.

The Effects of Inhalation of Smoke and its Treatment.—Dr. J. C. Da Costa, in his capacity as surgeon to the fire department, has had occa-

sion to treat a large number of firemen who have been exposed to vapor and smoke generated in burning buildings. Every fireman, while working inside a building, suffers more or less from smoke; even if not overcome, he is nauseated and often vomits. He always coughs and expectorates, is frequently dizzy, and his eyes invariably water and smart. For a day or two afterward, if he has been in dense smoke for any length of time, his eyes are red and irritated, his throat is sore, and he coughs up thick phlegm specked with visible pieces of carbon. He develops a tracheitis and bronchitis, and may have bronchopneumonia, and sometimes develops an œdema of the lungs. Some firemen learn how to "take smoke," and some stand it for a time with apparent indifference. Whiskey drinkers make bad firemen. Fat men, those suffering with heart disease, or those with laryngitis or chronic bronchitis, cannot endure smoke. Smoke is often better stood when the stomach is empty than when it contains a partially digested meal, and hot days are more trying to firemen than cold days. The author brings out the fact that there are great differences in smokes in different buildings, some smokes being worse than others. Among the worst forms of plain smoke he finds that the smoke from lumber, furniture, barrel-staves, peach-baskets, and paper is the worst. The smoke from chemicals, oils, varnish, wool, broom-straw, and spices is also hard to tolerate; that from hay, pitch, tar, and petroleum is not so offensive. The density of the smoke is of great importance in determining its toxicity. The presence of illuminating gas in smoke creates a deadly poisonous atmosphere before it reaches the explosion point. In the treatment of more severe cases, in which the fireman is carried out in a totally unconscious condition, his head hanging backward and his mouth open, with weak, fluttering pulse, cold extremities; dilated, fixed pupils, shallow respiration, twitching limbs, spasmodic tremors—for such cases treatment is often impossible; but in all cases the man should be laid upon a blanket, artificial respiration should be begun immediately, and if oxygen is at hand it should be administered; cold extremities should be actively rubbed, hypodermic injections of strychnine or atropine given, and a mustard-plaster placed over the heart. As soon as breathing has been re-established he should be wrapped up and taken to the nearest hospital. On reaching the hospital his clothes should be removed, his body and extremities rubbed with coarse towels. Warm blankets should be wrapped around him, and he should be surrounded with hot bottles, and be given an enema of hot saline fluid or hot coffee. A catheter should be used if he has not urinated. Artificial respiration is an extremely important feature in the very severe cases. In a man who has been overcome by illuminating gas the same line of treatment should be followed, and in addition to this he should be freely bled and have a hot saline solution infused into his veins. Transfusion of human blood is even more serviceable than that of saline fluid. Treatment of the eyes, the lungs, the larynx, all call for special symptomatic attention.—*Therapeutic Gazette*, 1903, vol. xxvii. p. 153.

Massage in Rebellious Constipation.—Dr. H. Koettleitz says that there is no question but that in many gastrointestinal affections, and especially those which have an underlying atonic cause, massage has great efficiency. It should, nevertheless, be relegated to a second position by the

clinician, but should not be entirely forgotten. With reference to the technique there are many things to be considered, but in general that of Hoffa is to be preferred. He reports a series of cases in which intestinal massage has proven of service.—*Annales de la Polyclinique de Paris*, 1903, vol. xiv. p. 49.

Goitre.—Dr. E. Marten Payne reports 6 cases of this disease, 1 of which was associated with an attack of acute myxœdema, and in 5 the treatment was successful with the use of thyroid extract. The paper is illustrated with photographs of three of the patients, and is an interesting contribution to the therapy of this disease.—*British Medical Journal*, 1903, No. 2203, p. 660.

Treatment of Puerperal Insanity.—Dr. E. W. White, writing that in view of the fact that many cases of puerperal insanity might be taken care of and fatal accidents avoided by careful treatment, says that as soon as the premonitory symptoms are observed—that is, a change of manner and of feelings, with excitability—quiet surroundings must be assured and skilful supervision of the patient enforced in order to guard against infanticide or suicide by impulse. Enemata and mild apperients are necessary for the regular bowel action, and if there is early insomnia a sedative mixture of one-half drachm of potassium bromide and chloral hydrate should be given at night. Liberal and sustaining diet is necessary. If there is added acute maniacal excitement, potassium bromide and chloral hydrate in the same proportion should be given twice or thrice daily. Its effect should be carefully watched, and it should not be continued beyond the stage of usefulness. Subsequently sulphonal or trional in 20-grain to 30-grain doses may be given with 1½ drachms to 2 drachms of paraldehyde. A malt-iron tonic may be given to treat the anæmia and albuminuria. Opium, he thinks, should be avoided in all maniacal conditions. If, however, the mental symptoms when fully established are of the maniacal type, the preparations of opium and advisable stimulants are indicated. He orders the liquor morphinæ acetatis (a 1 per cent. solution of morphine) 20 minims, spiritus ætheris 15 minims, in aqua camphoræ, one drachm thrice daily. Iron is given, and every effort made to re-establish by hot baths, aloes, ergot, etc., the suppressed menstrual function. A rapid loss of weight should be counteracted by olive oil, if possible, and alcoholic stimulants are of great benefit.—*British Medical Journal*, 1903, No. 2297, p. 806.

The Coal-tar Products in Neuralgia and Other Painful Conditions.—Dr. Wharton Sinkler gives a historical sketch of the introduction of the various coal-tar products—antipyrin, acetanilid, phenacetin and the other anilin preparations that have been produced in the last twenty years. Although marvellous powers have been ascribed to them, they are of value only in pains that have a nervous origin. The affections in which they have been found of greatest use are migraine and other forms of headache that are not organic; sciatica, lumbago; trifacial, intercostal, and other neuralgias; the pains of locomotor ataxia, and in ovarian and visceral pains. The occasional unfavorable effects in cases of idiosyncrasy are pointed out; the grave consequences of the aniline preparations being profuse sweating,

cyanosis, exhaustive oppression, and collapse. But the legitimate use of the coal-tar products has increased each year, and they are more relied on by the medical profession for the relief of pain than ever before.—*Therapeutic Gazette*, 1903, vol. xxvii. p. 4.

OBSTETRICS.

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Treatment of Placenta Prævia by Rapid Dilatation of the Cervix with Bossi's Dilator.—In the *Archiv f. Gynäkologie*, 1903, Band lix., Heft 1., DE-BAOLI reports 19 cases of placenta prævia in which Bossi's dilator was used to expedite delivery. He urges the use of this instrument in these cases in place of manual dilatation or Cæsarean section. It is claimed that in fifteen or twenty minutes the cervix is sufficiently dilated to permit the delivery of the child with no more laceration than is usually seen in spontaneous labor. He reports a maternal mortality of one only in these cases. In central placenta prævia he would dilate to between eight and nine cm. if the patient is near full term. Should bleeding occur during dilatation he endeavors to rupture the membrane. If this is not sufficient the hand is introduced and version is made, and the body of the child is used as a tampon. If delivery is attempted by forceps the instrument must be rapidly withdrawn, because the cervix will contract as soon as the dilator is removed.

In removing the instrument the index and middle fingers of the left hand should be placed upon the end of the branches while the instrument is raised and withdrawn by the right. The instrument is gradually closed to one cm. before withdrawal, and the fingers of the left hand follow the instrument carefully to see that no tissue is lacerated by its withdrawal. The uterus and vagina should be immediately tamponned with iodoform gauze as soon as the child has been delivered.

Rupture of the Uterus; Abdominal Section; Recovery.—FRASER (*Medical News*, June 27, 1903) reports the case of a multipara who had borne eight children in previous labors, and twice had adherent placenta. She had an old umbilical hernia, and was in charge of a midwife. During labor the midwife had put her fingers into the vagina to help the patient, and had passed them high up at one time, causing intense agony, after which labor entirely ceased. Great weakness and vomiting had followed.

On examination there was great tenderness on palpation all over the abdomen. The patient was vomiting dark green fluid, and labor pains had ceased. On vaginal examination the os was fully dilated, the cervix soft, the

posterior lip swollen and low in the vagina. On the posterior wall of the uterus above the os there was an abnormal opening. The head was above the brim, the vertex toward the right and posterior, and freely movable. On introducing the hand it came in contact with a coil of intestine. It was impossible to rotate the child's head, as the uterus rotated with it. The head could not be reached by forceps. It was possible to deliver by version, and this was done without much difficulty. The child was dead from separation of the placenta. On removing the placenta the intestine again prolapsed.

It was impossible to take the patient to a hospital, and, accordingly, the operation was done at the house.

The tear was on the posterior surface, extending completely across and to the left. The uterus was completely removed, the abdominal cavity irrigated with hot salt solution and packed with sterile gauze. This was carried down into the vagina, which was tamponned with iodoform gauze. The patient made a recovery complicated by vomiting, distention of the abdomen, and tenderness. The gauze was removed five days after operation.

The operation was done under very unfavorable circumstances, as the patient had been infected by a midwife and adequate assistance could not be procured.

The Maternal and Fetal Temperature.—CHAMPION (*Journal of Obstetrics and Gynecology of the British Empire*, June, 1903) has made observations in thirty-three cases to ascertain the maternal and fetal temperatures. The average temperature of the child at birth was 99.6° F. The average temperature of the mother was 98.6° F. Immediately after birth the child's temperature fell about 2°. The temperature of the child at birth varied between 97.4° and 101.2°, while the mother's temperature varied between 96.4° and 100.2°. The maternal temperature rarely fell to a considerable degree after delivery.

The temperature of the fœtus in utero must be higher than that of the mother. The loss of heat occurs from the skin and by the lungs. In no case was a bath given until the temperature had been taken.

Chorioepithelioma.—TEACHER (*British Medical Journal*, June 20, 1903) gave a demonstration before the Obstetrical Society of London on this subject. He believes that these tumors originate from the chorionic epithelium, which is of fetal epiblastic origin. They are distinct, and should not be classed as sarcoma or carcinoma. Hydatid mole should be considered a variety of this disease. In addition to these there are tumors not connected with pregnancy which may occur in either sex and in any organ. Such are probably teratomata.

Recent publications emphasize the fetal origin of malignant tumors which may attack either sex. Schlagenhaufer's case of malignant tumor in a male subject with metastasis in the lung strikingly illustrates this point (*Wiener med. Wochenschrift.*, May, 1902).

Two Cases of Fatal Eclampsia, with Premature Separation of the Placenta and Death during Labor. SEITZ (*Archiv f. Gynäkologie*, 1903, Band lxix., Heft 1) reports two cases of eclampsia in which hemorrhage occurred

during labor, followed by death. In the first case autopsy showed acute hemorrhagic parenchymatous nephritis, with parenchymatous degeneration of the myocardium. Œdema of the lungs was also present. On microscopic examination small-cell infiltration and degeneration of the vessels of the villi and decidua were present. From this occurred hemorrhage and infarction, with disturbance in the circulation and separation of the placenta.

In case second parenchymatous nephritis was also present, with small hemorrhages and necrosis in the liver and in the cortex of the brain. There was also tubercular infection in the lungs and lymph glands. In this case degenerative changes in the decidua and fetal membranes were found, and a large retroplacental hæmatoma caused by premature separation of the placenta.

Ferments in the Amniotic Liquid.—Bondi (*Zentralblatt f. Gynäkologie*, 1903, No. 21) has examined the amniotic liquid to determine the presence of ferments. Pepsin could be recognized, while trypsin could not. Autolysis in the amniotic liquid could not be recognized. In addition to pepsin diastasis was present. These ferments are also found in the serum of adults, although they are not present or in traces only in the blood serum of the newborn. As they are constantly present in amniotic liquid, they must come from the serum of the maternal blood. They have no influence upon the maceration of the dead fœtus. The changes which go on in the internal organs of the dead fœtus result from autolysis.

Facial Paralysis in the Fœtus after Cæsarean Section.—Vogel (*Zeitschrift f. Geburtshülfe*, 1903, Band xlvii., Heft 3) describes complete facial paralysis on the left side in a child delivered by Cæsarean operation. The pelvis was moderately contracted, and the child presented obliquely at the pelvic brim. The brow of the child was presenting. The pelvis was osteomalacic, and the left side of the child's head pressed upon a projection in the brim of the pelvis. The patient had strong labor pains before the operation was undertaken.

Pregnancy after Removal of Both Ovaries for Cystic Tumors.—Doran (*Transactions of the Obstetrical Society*, London, vol. xliv. p. 231) describes the case of a patient, aged twenty-five years, who had one child and then was operated on for the removal of a cystic tumor of the left ovary. She then had four children, and when thirty-nine years old had a cystic tumor of the right ovary removed. There was no evidence of ovarian tissue remaining. A small tubercle was left on the left side of the uterus. The patient afterward menstruated, and had a child two years after. She had symptoms later of the menopause, although these symptoms were very slight.

Ovarian tissue must have been present in these cases. It may remain a detached area in the ovarian ligament. Ligatures placed upon the tubes may ulcerate through, leaving the tube patent.

The Diagnosis of Extra-uterine Pregnancy.—Kober (*Zentralblatt f. Gynäkologie*, 1903, No. 22) concludes from his investigations of the subject that it is impossible to assert that all cases of hæmatocele result from ectopic

gestation. Wherever it is possible to recognize fetal tissue the diagnosis is plain. The histological examination is often difficult, and occasionally the positive result cannot be obtained. It is often more the result of good fortune than of the method of examination that fetal tissue is detected.

Injuries to the Child's Head during Delivery.—In the *Journal of Obstetrics and Gynecology of the British Empire*, June, 1903, JARDINE reports a number of cases of injury to the child's head through delivery. In one case the pelvis was normal, but the mother's abdomen was so pendulous that the head would not enter the brim. The child was large, and was delivered with axis-traction forceps. The frontal bone and part of the parietal on the right side were deeply furrowed. The child seemed to suffer no inconvenience from this injury.

In a second case, with normal pelvis, the depression was at the posterior portion of the right parietal bone, probably caused by the pressure of an ischial spine. This depression nearly disappeared. The frontal bone is often depressed, and after breech delivery the parietal bones are often considerably depressed. In many of these cases the bone rises to its normal position within a few years after the birth of the child.

Fracture may occur during delivery without evidence of depression. This is usually seen in difficult forceps delivery, often through contracted pelves. In one case the mother had rickets, with a diagonal conjugate of four inches. Her first child had been delivered by forceps. Considerable traction was required, and as the head passed the promontory there was an evident thud. The child was living, but had a marked depression of the frontal bone. Very firm pressure failed to raise the depression. When the child was twelve days old an incision was made through the bone and the depressed portion raised with a periosteum elevator. The incision was made away from the suture, as the dura is always adherent at the suture. When the elevator was introduced there was a gush of blood-stained serum. Considerable force was required to raise the depressed bone. The child did well. Slight flattening of the bone remained, but the condition was greatly improved.

Hemorrhage may occur in cases where the bone is intact. A case is described in which a large child was delivered by version. The child had convulsions soon after birth, and became hopelessly imbecile. In a second case a child delivered by forceps has been slow in walking and in development.

Injury to the eyes may vary greatly in severity. Keratitis may develop and be mistaken for keratitis of cengenital origin. In some of these cases considerable hemorrhage into the conjunctival sac was present and in others the elastic lamina of the cornea was ruptured in several places.

Chorea in Pregnancy.—WALL and ANDREWS (*Journal of Obstetrics and Gynecology of the British Empire*, June, 1903) have collected forty cases of chorea during pregnancy. So far as causation is concerned the instability of the nervous system seen in pregnancy is a factor, while rheumatism often precedes chorea. In one case of microcephalus congenital deficiency of the brain was undoubtedly a factor. Anxiety over confinement or other depressing emotion may produce chorea in a pregnant patient. In one case a pregnant woman became choreic after seeing a man attempt to cut his throat.

In the forty cases chorea occurred during the first pregnancy in eighteen. In ten cases the first pregnancy was free from chorea, but chorea occurred in later pregnancy. There was a history of previous chorea in twenty-three cases, and in six chorea recurred in subsequent pregnancies. Chorea was most apt to happen between the fourth and fifth months, and next in frequency between the second and third, fifth and sixth, and seventh and eighth months. There were two spontaneous abortions, and in two the uterus was empty. There were five fatal cases, and two of these had spontaneous abortion.

It is believed that the importance of insanity as inducing chorea has been much exaggerated. It is also observed that chorea does not necessarily tend to recur in subsequent pregnancies.

The treatment of chorea during pregnancy consists chiefly in good nursing, full feeding, and in securing quiet and sleep. Cause for worry must be removed. Light massage is often useful. Large doses of bromide are very injurious. Alcohol is decidedly of value, and if a sedative must be employed chloral hydrate or chloralamide are probably best. The induction of abortion should be very seldom practised.

GYNECOLOGY.

UNDER THE CHARGE OF

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Successful Abdominal Section.—MARSCHNER (*Zentralblatt für Gynäkologie*, 1903, No. 19) reports a series of 125 cases, with no deaths, the majority being complicated. These include 22 myomectomies, 17 ectopies, and 17 cases of pyosalpinx. Drainage through the abdominal wound with iodoform gauze was employed in over 40 per cent. Two of the patients with ruptured ectopie were nearly pulseless when received into the hospital, and in one instance a second laparotomy for intestinal obstruction was necessary ten days after the first. The writer prefers the abdominal to the vaginal route even for the removal of small ovarian cysts and fibroid.

Salpingitis Following Injection of Chloride of Zinc.—WEISSWANGS (*Zentralblatt für Gynäkologie*, 1903, No. 19) reports the case of a young woman with obstinate menorrhagia, who was curetted repeatedly without benefit. After the last curettement a solution of chloride of zinc was injected into the uterus with Braun's syringe. Five days later, the diagnosis of cancer having been made, vaginal hysterectomy was performed and acute salpingitis was found to be present, due to sloughing of the endometrium at the fundus, which had extended into the tubes. Adenocarcinoma was present.

The writer concludes not only that tissue removed by the curette should always be examined microscopically, but that intra-uterine injections of chloride of zinc are never free from danger.

In the discussion of this case before the Dresden Gynecological Society, Leopold recalled three other fatal cases in the practice of a colleague, and expressed surprise that the instrument was still in use, and this seemed to be the general sense of the Society.

Examination of the Appendix in Every Abdominal Section.—Weiss-wangs (*Zentralblatt für Gynäkologie*, 1903, No. 19) insists upon the importance of inspecting and removing the appendix whenever the abdomen is opened, and reports a case in which, after extirpating an ovarian cyst, he discovered an inflamed appendix, which contained tooth-brush bristles and was on the point of undergoing perforation. In a former case he had been obliged to operate for the removal of an appendix which he had spared at a previous operation.

Pseudohermaphroditism.—Heugge (*Monatsschrift für Geb. u. Gyn*, Band xvii., Heft 1), in reporting two cases, draws the following conclusions: 1. There are frequent exceptions to the rule that the physical and psychical characters of sex are dependent upon the sexual organs. 2. The earlier the change in these organs, the greater the change in sexual peculiarities. 3. Mechanical causes should always be sought for to explain congenital changes in the genitalia and disposition; and when these cannot be discovered some trophic or nervous influence must be inferred. 4. Education and example exert a strong influence on the sexual character as well as other influences, such as dysmenorrhœa in male pseudohermaphrodites. 5. He advises removal of the ovaries in these subjects only when they are the seat of severe pain or when through absence of the external genitals the former cannot perform their functions.

Fibroma of the Ovary.—Hunner (*Johns Hopkins Hospital Bulletin*, vol. xiii., No. 139), in reporting a case of large fibroma of the ovary with twisted pedicle and extensive ascites, calls attention to the fact that the diagnosis of malignant and inoperable tumor would usually be made under these circumstances.

The writer notes that only nine ovarian fibroids were found out of 9400 operative gynecological cases at the hospital. In six uterine fibromyomata were also present. Ascites was noted in four instances, in which there was evident disturbance of the venous circulation, due to either torsion of the pedicle or subperitoneal development of the growth.

Cause of Twisted Pedicle.—Payr (*Archiv für klin. Chirurgie*, Band lxviii., Heft 2) reports a case of ovarian cystoma which had become almost completely separated from the uterus in consequence of torsion of the pedicle. An extensive omental adhesion had undergone a similar twisting and attenuation. The writer conducted a series of experiments in animals with the view of explaining this phenomenon. Aside from the recognized causes —peristalsis, changes in the fulness of the intestines, contraction and flabbi-

ness of the abdominal muscles, abdominal pressure, and sudden change of position of the body—the size, weight, and consistence of the tumor are important factors. Extreme venous stasis may favor or even cause torsion.

Simultaneous Development of Cancer in the Uterus and Ovaries.—FUNK (Inaugural Dissertation; Abstract in *Zentralblatt für Gynäkologie*, 1903, No. 19) reports four cases in which an examination of the periuterine tissues showed no evidence of direct extension of the disease from the uterus to the ovaries. He regards these as very rare, since cancer generally originates in the uterus and extends to the ovaries through the lymphatics. The four patients were operated upon successfully, but a recurrence was to be expected.

Circular Vaginal Suture in Retroflexion.—SCHÜCKING (*Zentralblatt für Gynäkologie*, 1903, No. 23) calls attention to the fact that in movable retroflexion it is often possible to keep the uterus anteverted by means of a pessary so small that it can have no supporting power. This he explains by reference to the fact that when the position of the uterus is changed from anteversion to retroversion the posterior vaginal fornix must descend and fold together. This is prevented by the pressure of the pessary. This may be prevented equally well by a buried suture which surrounds the vaginal vault. The operation, which does not require anæsthesia if the vagina is roomy, is performed as follows: A buried silkworm-gut, or, better, silver-wire suture, is carried around the portio vaginalis from left to right, the needle emerging at the point of entrance. If the posterior vaginal vault is much relaxed, as many as six sutures may be used, and are left *in situ* for from four to six weeks. From an experience with a series of successful cases the writer has found that there result two lateral and one posterior cicatrices, which oppose considerable resistance to stretching of the mucous membrane, prevent the formation of the fold before mentioned, and thus keep the uterus anteverted. Until the scars have become sufficiently firm, it is advisable to replace the uterus frequently, or, better, to insert a pessary for a few weeks.

Adhesions after Abdominal Section.—VOGEL (*Deutsche Zeitschrift für Chirurgie*, Band lxiii.), from a series of experiments in rabbits, finds that peritoneal adhesions may be due to the following factors: (1) effusions of blood; (2) mechanical injuries, especially if extensive and at a distance from the abdominal wound; (3) slight burns as contrasted with deep destruction of tissue by heat; (4) chemical irritation; (5) foreign bodies; (6) infection. After ligation of omentum the stumps were always found to be adherent. Omental adhesions were sometimes noted along the line of an aseptic wound, but never healthy intestine. These were least apt to form when silver wire was used as suture material. Adhesions were more apt to form when the bowels were constipated, the reverse being true when the animal was allowed to eat and move about immediately after the operation. Practically the prevention of adhesions is best attained by the avoidance of mechanical injury to the peritoneum, of a too thorough toilet after the escape of blood or cyst fluids, or of the use of the Paquelin cautery, together with early peristalsis. This is especially important after an operation for intestinal obstruction.

In his experiments the writer promoted early peristalsis by diet and subcutaneous injections of atropine and physostigmine. In order to render the serous covering of the intestines slippery, he injected into the peritoneal cavity a mixture of egg albumen, mucin, and gum arabic in sterilized salt solution. From eight to ten ounces of this solution were poured into the cavity; then adhesions were produced by placing a sterile gauze pad among the intestines. From four to eight days later the pad was removed, the adhesions were separated, and more of the "slippery" mixture was introduced, while injections of physostigmine were given. This treatment always prevented adhesions from forming, even when eschars and omental stumps were present.

The writer has relieved ileus in the human subject after laparotomy with subcutaneous injections of physostigmine salicylate, gr. $\frac{1}{150}$, repeated six times in five days without unpleasant symptoms. He also recommends frequent changes of position after the fifth day and abdominal massage, with light gymnastics during convalescence. In order to prevent the union of adjacent serous surfaces, he would even leave within the peritoneal cavity a lubricating solution such as he used in his experiments.

Changes in the Endometrium in Acute Infectious Diseases.—STRAVOSKIADIS (*Zentralblatt für Gynäkologie*, 1903, No. 20) reports the results of his examination of twenty-four uteri from patients dying with acute croupous pneumonia, typhoid, and other infectious diseases. He found the following changes in the uterus: 1. Acute endometritis, sometimes hemorrhagic, is common. 2. This inflammation is caused by the specific bacteria which are usually regarded as the cause of the general disease, except in cases in which a complication arises, when the endometritis may be referable to the same factor which originated the complication. 3. The bacteria reach the uterus through the bloodvessels, their development being especially rapid in the pregnant or puerperal organ. 4. Abortion or premature delivery during the course of an acute infectious disease is often referable to such an endometritis of bacterial origin.

Drainage.—HOFMEIER (*Zentralblatt für Gynäkologie*, 1903, No. 8) reconsiders at length this important subject, his conclusions being based upon thirty cases selected from 216 laporotomies. Eight were drained and twenty-two were not. Only one of the latter was fatal. In general he is opposed to drainage, and believes that it is difficult to prove its advantages in a given case. It may be regarded as an extra safeguard and does no harm. Vaginal gauze drainage is the most natural method after hysterectomy, but should seldom be employed if the uterus is not removed. A glass drain is nearly always preferable to gauze in the abdominal wound.

Fixation of Prolapsed Bladder.—CHIAVENTONE (*Obstétrique: Zentralblatt für Gynäkologie*, 1903, No. 5) describes an ingenious operation which is based on the theory that cystocele does not represent prolapse of the entire bladder, but only of the base, the anterior and posterior walls being simply overstretched; hence elevation of either wall does not influence the prolapse.

The writer believes that abdominal section is indicated in all severe cases

of cystocele. He dissects off the vesico-uterine fold of peritoneum and separates the base of the bladder from the cervix as low down as the inter-ureteric ligament and base of the trigone, where the attachment is most intimate. The bladder is then sutured to the anterior surface of the uterus one-half inch higher up than its original site, and ventrofixation is performed. The ureters must be carefully avoided.

DERMATOLOGY.

UNDER THE CHARGE OF

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Etiology of Acne Vulgaris.—T. C. GILCHRIST (*The Journal of Cutaneous Medicine*, March, 1903), after alluding to the work done in this direction by Unna in 1893, Hodara in 1894, Lowry in 1896, and Sabouraud in 1894, makes the statement that "up to 1899 no observer had succeeded in obtaining the acne bacilli pure from lesions of acne vulgaris or comedo, and there was practically no proof that these bacilli were the cause of acne vulgaris." The author then directs attention to his own published work on this subject in 1899, and concludes from more recent investigations that definite bacilli (bacillus acnes) were present in all smears taken from 240 typical acne lesions from 86 patients. Pure cultures were obtained from 62 lesions (chiefly acne nodules) from 29 patients. It is present as a short, thick bacillus in smears, but in culture often becomes much longer and thicker, and in old cultures assumes distinct branching forms. He considers it definitely proved that this micro-organism is the primary cause of acne vulgaris.

A Case of Blastomycosis.—J. H. SEQUEIRA (*British Journal of Dermatology*, April, 1903) describes a case (with illustrations) of this rare and new disease, affecting chiefly the region of the lower eyelids, occurring in a strong, healthy man, aged thirty-seven years. The clinical appearances and the results of pathological examination exclude rodent ulcer, epithelioma, and other neoplasms of the skin, and also lupus and other granulomata. The diagnosis was based on the following points: 1. The face and scalp alone were affected. 2. The lesions were multiple. 3. These spread and fresh lesions appeared apparently by inoculation. 4. The edges of the tumors were well defined, and there was but little infiltration. 5. They soon became pustular, and thin, whitish pus could be squeezed from the lesions. 6. Microscopically there were numerous minute epidermal abscesses 7. In these abscesses and in the pus squeezed from them budding yeast-like

organisms were found. 8. From the deeper layer of the epidermis, branching-down growths of prickle-cells were found extending into the corium. The growths were markedly influenced but were not entirely dispersed by potassium iodide in large doses.

On Spontaneous and Scar Keloid.—M. A. CHLENOV (*British Journal of Dermatology*, April, 1903, p. 156), after discussing the views held by observers as to the nature and classification of keloids, describes a case of spontaneous keloid in which there were 431 growths, fourteen being upon the genital organs. Baths (93° to 100° F.); inunction with 30 per cent. resorcin ointment; hypodermic injections of arsenic (60 injections of a 1 per cent. solution), and phototheraphy by means of a Lortet-Genoud lamp (but only two treatments to two tumors) were employed. The resorcin ointment seemed to soften the tumors, and the light treatment had no effect on one tumor, but the other grew distinctly larger. The author concludes that hypertrophied scars should not be included among the keloids; that the distinction between primary and secondary keloids cannot be strictly maintained; that the histological changes in keloid growths consist in hypertrophy of the fibrous tissue (with destruction of the elastic tissue) along the bloodvessels; that the chief cause of the appearance of keloid is a special predisposition of the individual, family, or race; and, finally, that the treatment is unsatisfactory. [The long-continued use of the Röntgen rays can be commended in keloid.—L. A. D.]

Tinea Favosa Capitis Successfully Treated with Izal.—D. DUCKWORTH (*St. Bartholomew's Hospital Reports*, vol. xxxviii., 1902, p. 155) considers, from the treatment of two marked chronic, rebellious cases with this drug, that it possesses distinct advantages over most other parasiticides. Though a stimulant, and may prove an irritant, it is non-toxic. It was employed as a 50 per cent. ointment with lanolin in one case, and with glycerin and water in the other case. Improvement began in a few weeks, and the cures seemed to have been permanent in both instances. The hair grew in again except in the originally bald areas.

Lupus Treatment by Lang's Hot-air Method.—L. SPITZER (*British Journal of Dermatology*, April, 1903) states that Lang's apparatus is similar in principle to Paquelin's cautery, and is heated by benzine, and that the treatment is not followed by unpleasant consequences to the patient. Its advantages are: rapid healing; good cosmetic result, the scars being smooth, soft, and supple; possibility of application to even large areas; and the simplicity and ease of application. Should more than one treatment be necessary, there may still be hope of a successful result and permanent cure.

A Diagnostic Examination of One Hundred and Fifty Cases of Leprosy.—J. T. MCDONALD, of Hawaii (*Journal of the American Medical Association*, June 6, 1903), first states that the disease in Hawaii is on the decline, thus proving the value of segregation, established over thirty years ago. The method of apprehending and dealing with leper suspects and other practical points are referred to in detail. The following is a summary of the article: 1. The microscope is the chief agent in the final diagnosis of leprosy.

No patient should be committed to a segregated colony without a bacteriological demonstration of the disease. 2. Of clinical symptoms, macules chiefly leucodermic spots, are found in 89 per cent. of all cases. 3. The leprosy nodule found in 74 per cent. is the one chief distinguishing lesion of skin leprosy. 4. Thinning or complete loss of eyebrows and lashes is present in 63 per cent. 5. Atrophic changes in hands and forearms, with retraction and contraction of fingers and enlarged ulnar nerve in 32 per cent., a leading feature of nerve leprosy. 6. The plantar ulcer, found in 26 per cent., usually on the ball of the foot. 7. Absorption of phalanges in 16 per cent., with occasional spontaneous amputation. 8. Elephantiasis of hands and feet in 16 per cent. 9. Facial paralysis in 11 per cent. 10. The entire body should be carefully tested for anæsthetic areas. 11. Several of the above symptoms can be found, in some slight degree at least, in every leprous subject.

Favus of Scrotum Co-existing with Ringworm of Thigh: Identical Trichophyton-like Cultures.—A. D. MEWBORN (*The Journal of Cutaneous Diseases*, January, 1903) discusses the subject of the cultures of the achorion Schönleinii and the trichophyton fungus, and concludes that this case may be regarded as one in which the same trichophyton (a megalosporon ectothrix, of probable animal origin) on the same patient, but in different parts of the body, where the conditions of soil were different, produced two clinically distinct diseases, viz., favus and ringworm.

The X-rays in Lupus, Rodent Ulcer, and Other Skin Diseases.—MORRIS and DORE (*British Medical Journal*, June 6, 1903), who have, on a previous occasion, given their views in the same publication, conclude from more recent work that the X-ray treatment, while it has a well-defined sphere of usefulness, is, in the case of lupus vulgaris, much inferior in curative efficacy to Finsen's light treatment. The use of the X-rays, however, supplies certain deficiencies of the Finsen light treatment, as they can be applied to cavities inaccessible to the latter. In the treatment of lupus of mucous membranes the X-rays are more effective, and also for the healing of ulcerated areas, as well as for the relief of pain. As to the permanency of the good results obtained, opinions must be cautiously expressed. In rodent ulcer, relapses, after a varying period, are the rule.

The Red-light Treatment of Smallpox.—NIELS R. FINSEN (*British Medical Journal*, June 6, 1903) asks: Is the treatment of smallpox patients in broad daylight warrantable? Ten years ago he advocated the use of red light in the treatment of this disease, since which time it has been employed by many physicians in many places, meeting everywhere with unquestionable success, but the method to be successful must be properly conducted. It may be considered an irrefutable fact that daylight, and especially the chemical rays, have a most injurious effect on the course of smallpox, as the suppuration of the vesicles is due to the effect of light. On the other hand, light seems to have no action on the smallpox infection itself, and death caused by the latter cannot be prevented by excluding the chemical rays. But the avoidance of suppuration is in itself of the greatest importance, for

it is a well-known fact that the suppurative stage is the most dangerous of the several stages of smallpox; moreover, the greatest number of deaths are due to suppuration, which, other things being equal, would be prevented if no suppuration were present. The action of light on the course of smallpox is astonishing, and the effect of the red-light treatment is one of the most striking results known in medicine; but if suppuration has begun, or is on the point of beginning, the red-light treatment will not stop it. Unless an epidemic of smallpox is of an exceptionally fatal character, the death-list may be reduced 50 per cent. by the employment of this treatment over the treatment in broad daylight. [The method referred to has been exploited in detail by Finsen in numerous publications, especially in his work on *Phototherapy* published in English, London, 1901. The author asks that a commission be appointed in Great Britain to investigate the correctness of his statements on the value of this treatment.—L. A. D.]

Radiotherapy in Diseases of the Skin.—H. R. VARNEY, of Detroit (*Journal of the American Medical Association*, June 6, 1903) in an interesting article on "Results in Radiotherapy," gives his experience with a number of cutaneous diseases, including twelve cases of lupus treated from 1900 to 1903, 10 of which were clinically cured, no other treatment than the rays being given. Most gratifying results were obtained in acne, but only the indurated pustular form of the disease, that had proved rebellious to all remedies, was treated. If the treatment is carried to the point of a production of erythema and stiffening of the skin, the peeling which follows will aid in the removal of pits and scars from old lesions. There was no recurrence in these cases. After long treatment with two cases of hypertrichosis, the author is not favorably inclined to its use in this disease. Experience with keloid and verruca has been favorable, and the same remark applies to patches of infiltrated eczema. Sycosis has yielded rapidly and with gratifying results; so also have the pittings from smallpox, though by no means so rapidly. A case of diffuse scleroderma disappeared in a short period, with only a slight tendency to recurrence.

The X-ray and the Finsen Light in Lupus.—A. D. ROCKWELL (*Journal of Cutaneous Diseases*, June, 1893, p. 296) thinks that a positive answer as to which of these two methods of treatment in lupus is the better cannot be given at present. In one case of long standing that had resisted the Finsen light, a cure resulted from fifty-five exposures to the X-rays in a period of four months. Personal idiosyncrasy and the judgment of the operator must decide the choice of the agent.

Tinea of the Nails in Iceland.—PERNET (*British Journal of Dermatology*, March, 1903, p. 106) demonstrated the parasite in finger-nail scrapings, the disease being common in Iceland, where it is contracted from sheep, one or two out of every ten peasants suffering from it. Ehlers, of Copenhagen, pointed out the parasitic nature of this disease, called in Iceland "kartnegluer" (from kart, card for combing out work, and negluer, nails). The specimen showed the mycelium, which, in some preparations, was very profuse, especially in scrapings from the under surface of the nails.

PATHOLOGY AND BACTERIOLOGY.

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Infectious Epithelioses and Epitheliomata.—BORREL (*Annales Pasteur*, xvii., 1903, 81) reviews the studies of coccidial and other diseases in animals which are characterized by epithelial proliferation, to which much interest has been given in recent years on account of their possible parasitic etiology in common with cancer. Under the title of "Infectious Epithelioses" the author has grouped several diseases, such as sheep-rot, vaccinia, variola, aphthous fever, bovine pest, and molluscum contagiosum, in which the lesions show epithelial proliferation and the presence of so-called sporozoa which have been described under various names by different authors. A careful study of these lesions shows that they are practically identical; studies on the fresh tissue and fluid and in stained preparations give no evidence that the so-called sporozoa are in reality living organisms, but shows that they are in all probability disintegrated leucocytes. Hitherto the field of contention on the parasitic nature of Guarnieri's vaccine bodies has been the corneal inoculations, but Sikovsky has recently shown that similar bodies can be produced in the cornea with heated vaccine, rabbit serum, or diphtheria toxin. Furthermore, the virus of all but two of the mentioned diseases have been shown to retain their infective power when passed through a Pasteur filter. All these facts lead to the suggestion that these epithelioses may be caused by micro-organisms at present invisible. A comparison of these lesions with the epitheliomata of mice shows similar conditions and suggests the need of further research along the possible bacterial origin of cancer. The possibility of a serum therapy has already been undertaken by the author, but as yet the results do not warrant a communication on this most important phase of the question.

Experimentelle Beitrage zur Pathologie des Blutes.—DR. P. SCHMIDT (*Fischer, Jena*, 1902), in this monograph of thirty-nine pages, sketches a series of investigations as to the nature and significance of the basophilic granules in the red blood corpuscles first described by Askanazy in a case of progressive anæmia and later found in many cases of severe anæmia, in particular those due to lead intoxication. Schmidt's conclusion as a result of clinical observation and experiment is that the granules are a

sign of regeneration of red cells and not of degeneration as maintained by Grawitz and others; and are thus of the same significance as polychromatophylic and nucleated red corpuscles. These three types of "young" red cells are often found in association. Schmidt's crucial experiment is rather an ingenious one. He is able to find the granules in the circulating blood of the rabbit fifteen minutes after the subcutaneous administration of phenylhydrazine; if even as late as six hours after the injection of the drug he clamps off one ear completely from the circulating blood, he obtains in due time the granules in the red cells of the general circulation, but not in those of the blood of the ear. Similarly after venesection in a rabbit the circulating blood showed polychromatophilic and nucleated red blood cells, while that of the isolated ear remained unchanged. Defibrinated blood treated in test-tube with phenylhydrazine showed signs of disintegration of the red cells, but no basophilic granules. On exposure of an isolated rabbit's ear to the Finsen rays no demonstrable change was noted in the stained blood smear, though the tissues of the ear were markedly affected. These experiments are held to indicate that the basophilic granules are not the product of protoplasmic degeneration. The toxic agent acts like venesection in removing red blood cells from the circulation. There is excessive demand on the bone-marrow, and immature red cells are thrust into the circulating blood; some show complete nuclei, others pyknotic fragments of nuclei, and all transitions to the fine basophilic granules—while others, the polychromatophilic, the author holds, show the result of karyolysis. The granules, then, are derived from the nucleus, and are either thrown off during the mitotic process or are a product of the nuclear degeneration.

Experimental Study of Sheep-rot.—BORREL (*Annales Pasteur*, xvii., 1903, 123) finds that the filtration of sheep-rot pus through a Berkefeld or an ordinary Chamberlain filter will give a filtrate which contains an active virus. There is no organism visible in cover-slips and no growth is obtainable on the ordinary culture media. The presumption is that an ultramicroscopic bacterium is the cause of the disease. Rams highly immunized with the virus give a serum which when mixed with the virus will prevent the evolution of the characteristic pustule and the generalized course of the disease. Such immune serum in several instances has also been used to cure animals in a diseased herd. The cure and prevention of a disease which is of considerable significance seem assured.

Fixation of Tetanus Toxin by Brain Substance.—BESREDKA (*Annales Pasteur*, xvii., 1903, 138) has repeated the experiments of Wassermann and Takaki on the neutralization of tetanus toxin by brain substance which have been used as affirmative data of the Ehrlich "lateral chain" hypothesis. Besredka considers that the fixation of the toxin by the brain has been used as confirmative of the presence of antitoxin in the brain substance. He shows that when tetanus toxin and brain tissue are ground together the mixture does separate all the toxic principles from the supernatant fluid, but that the saturated emulsion is in itself as toxic as the toxin alone. The further addition of tetanus antitoxin removes the toxin from the brain substance and neutralizes it. The brain is subsequently capable of absorbing

new amounts of toxin. This proves that the brain itself does not contain a true antitoxin, since it does not neutralize the effects of the toxin. The affinity which exists in brain cells is furthermore not so active as true tetanus antitoxin, since the subsequent addition of this antitoxin will separate the toxin from the brain tissue.

Experimental Tumors.—LECENE and LEGROS (*Bull. de la Soc. Anat. de Paris*, No. 8, 1902, p. 764) report on the results of including pieces of fresh embryonic guinea-pig organs subcutaneously in adult guinea-pigs. Small bits of kidney, adrenal, or both organs were placed under the skin, closed in and left for from fifteen to forty days. Out of six attempts, two gave positive results of the following order: cyst-like tumors were found composed of the enclosed embryonic tissue which had grown distinctly in size and infiltrated the surrounding connective tissue. In both cases the cells histologically were normal in appearance, and in one case the tumor resembled a mixed tumor of the ovary or testicle.

A Study of a Bacillus Resembling the Bacillus of Shiga, from a Case of Fatal Diarrhœa in a Child; with Remarks on the Recognition of Dysentery, Typhoid, and Allied Bacilli.—HISS and RUSSELL (*The Medical News*, 1903, 289) isolated from a fatal case of enterocolitis in a child an organism which presents many points in common with the bacillus of Shiga which is now generally recognized as the cause of acute dysentery. What is undoubtedly the same organism has since been isolated by Flexner, Kruse, and others. Lately Martini and Lentz have claimed that there is a difference between the species Flexner and the true Shiga bacillus on the basis of slight variations in agglutination and the different reaction on mannite litmus agar. The organism isolated by the authors (Bacillus "Y") grows on the ordinary media and sugars as does B. dysenteriæ. On mannite, however, it produces acid, as is shown in both the litmus medium of Lentz and in the serum water medium of Hiss, in this respect resembling B. typhosus and differing from the Shiga strain of B. dysenteriæ. Agglutinations with normal horse serum (Flexner) and antityphoid serum are positive. The serum of a rabbit highly agglutinative for B. "Y" fails to agglutinate the various strains of B. dysenteriæ, but agglutinates distinctly B. typhosus. The results with this organism suggest the possible errors of diagnosis by agglutination as well as mistakes in the identity of an organism based on insufficient cultural data.

Emergency Report on Surra.—SALMON and STILES (*Bull. No.* 42, *Bureau of Animal Industry*, Washington, 1902) have published this report on a disease which has already been much studied on account of the diagnosis of its occurrence in the Philippines by Smith and Kinyoun and the subsequent prohibition of landing animals from these islands at any port in the United States. Surra is a specific and continuous febrile disease occurring in horses, camels, and other domestic animals. The disease is caused by a microscopic, flagellated parasite, the Trypanosoma Evansi, and is easily transmitted by inoculation, the transmission being almost entirely due to the biting of flies of the genus Tabanus (horse flies). Parasites closely allied in species occur

in nearly all parts of the world, and in some cases cause similar diseases, such as tse-tse fly disease, dourine, mal de caderas, and rat trypanosomiasis.

The disease surra occurs more frequently in wet weather and is invariably fatal. Treatment is most unsatisfactory, arsenic alone having yielded fair results in certain cases. Immunization has as yet been entirely unsuccessful and prevention is difficult, and to be successful must consist in protection from flies. The symptoms of surra are fever, remittent or unremittent in type, and often relapsing urticaria, petechia on mucous surfaces, œdema and progressive anæmia, and emaciation followed by death in from forty to sixty days. The introduction of the disease into the Philippines is uncertain, but it has probably existed there some time. Its introduction, from a military and economic standpoint, into the United States, would be a serious matter in view of its great lethality. A careful consideration of allied diseases together with their individually causative parasites, is incorporated in the text and the report is followed by a complete bibliography of the entire subject by Hassall.

The Role of the Toxins in Inflammation of the Eye.—RANDOLPH (*Bulletin of the Johns Hopkins Hospital*, 1903, xiv. 47) finds that continued instillations of the toxins of B. diphtheriæ, gonococcus, streptococcus, staphylococcus aureus, and B. xerosis, produced by filtration of sugar-free bouillon cultures of varying ages, produced no reaction on the normal conjunctivæ of rabbits. If, on the contrary, small amounts of the filtrates from even most recent cultures were injected into the tissue of the conjuntiva, marked inflammatory reaction followed. This is of interest as indicating that the bacteria which are causative of conjunctivitis are probably dependent in their action upon some lesion of the conjunctiva. This conjunctival method of inoculation is of further interest, as it serves to detect toxins in certain bacteria which had hitherto not been supposed to produce extracellular toxins. A study of the bacteriology of the normal rabbit's conjunctiva showed that cocci are always present.

The Free Receptors of B. Typhosus and B. Dysenteriæ and Dysentery Toxin.—NEISSER and SHIGA (*Deutsche med. Woch.*, 1903, xxix., No. 4) have succeeded in separating the active immunizing principles (free receptors) from cultures of B. typhosus and B. dysenteriæ. These toxins are made by suspending a twenty-four hour agar culture of the organism in saline solution for one hour, killing the bacteria by heat, and, after letting the solution stand at 37° C. for two days, filtering through a Reichel filter. The bacteria-free filtrate contains the active bacterial receptors, for it will inhibit the normal agglutinating power of the specific immune serum, and when injected into animals will give rise to agglutinins and active bacteriolysins in the animal's blood. This method offers great advantages in the case of the B. typhosus, as these filtrates are free from the harmful effects which are caused by injections of vaccines composed of the dead bacilli. In the case of the dysentery filtrates a dose of 0.5 c.c. into a rabbit will cause diarrhœa and death with eliminative lesions of the small intestine.—F. P. G.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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Are Cows Susceptible to Typhoid Fever?—Epidemics of milk typhoid are well recognized phenomena, but have always been ascribed to the direct contamination of the milk with specifically polluted water. The investigations of Dr. Klein in connection with the classical outbreak of scarlatina in the districts of London supplied by Panter's dairy at Hendon left no doubt as to the disease among the cows being essentially scarlatina, though the external appearances differed greatly from those of the disease in man, the eruption being vesicular and pustular instead of a mere erythema; and the question has often been raised of the possibility of cows being affected by typhoid fever in a form so modified by the differences in their organism as to escape recognition, though capable through their milk of reproducing the fever in man. An observation recorded in the graduation thesis of Dr. E. Jacobsthal (Strassburg, 1902) constitutes the first contribution, though by no means a decisive one, to the solution of the question. In the pus contained in an abscess in the spleen of a cow killed in the public slaughter-house at Strassburg bacilli were found not only morphologically indistinguishable from those of enteric fever, but answering to all bacteriological and agglutination tests, with the serum of rabbits immunized thereby, and also with human typhoid bacilli, directly and reciprocally, in various dilutions. The question remained, however, unsolved whether this abscess was a sequela of a previous attack of unrecognized fever or was simply a local effect of the ingestion of the specific poison and its absorption by the lymphatics.—[E. F. W.]

The Etiology of the Summer Diarrhœas in Infants.—A preliminary report of their study of the bacterial flora of a number of cases of summer diarrhœa in infants has been made by DRS. C. W. DUVAL and V. H. BASSETT (*Centralblatt für Bakteriologie*, December 22, 1902, p. 52). In 42 typical cases they succeeded in isolating the Shiga bacillus of dysentery. They secured the specific organism also from scrapings of the intestinal mucosa at autopsy, and in one case from the mesenteric glands and liver. In the stools of acute cases the organism was often present in large numbers, but in those of mild cases and those of long duration it was secured with difficulty, because of its presence in relatively small numbers and also because of the antagonism of the normal intestinal bacteria. The specific bacilli isolated from different cases proved to be identical and to agree in all ways with those isolated from cases of acute dysentery in adults by Shiga in Japan, Flexner and

Strong in the Philippines, Kruse in Germany, and Vedder and Duval in this country. It was not found in the stools of twenty-five healthy children, nor in those of simple diarrhœa, marasmus, and malnutrition. Agglutinative reactions were obtained when the organisms were tested with (1) blood serum of patients from whom they were secured, (2) the serum of other infants suffering with summer diarrhœa, (3) the serum of patients with acute dysentery, and (4) with antidysenteric immune serum, but not with the blood serum of healthy children. They conclude that the summer diarrhœa of infants is etiologically identical with the acute bacillary dysentery of adults.

Nitrites in Water.—According to DR. SAMUEL RIDEAL (*Journal of State Medicine*, June, 1902), nitrites may be derived from four sources: (1) the soil, (2) the air, (3) oxidation of ammonia, (4) reduction of nitrates. The first two are consistent with the absence of organic matter and the presence of no bacteria or of only the innocuous atmospheric kinds. Compounds of ammonia and nitrates and nitrites are known to be very stable in dilute solutions free from the organisms that produce change, and therefore any of them may exist in organically pure water. It is the transformation from one to the other that is a suspicious sign. The third source of nitrites indicates really an improvement in the water, because nitrites in this dilution are quite innocuous and are susceptible of still further oxidation. The rapidity of the change is illustrated by the fact that the micrococcus isolated by Richter produced a nitrite reaction in fresh urine in twenty minutes. The organism "Nitrosomonas" oxidizes ammonia to nitrite without requiring for its nutriment any other carbon and nitrogen than it derives from air and from carbonates; consequently it can form nitrites in water organically pure. The fourth source has been elaborately studied. Nitrites can be formed and can persist in solutions almost free from organic matter, as in the case of the common organism "Nitrobacter." It is true that most bacteria which transform nitrates to nitrites require the presence of fermentable carbonaceous substances, and that this change usually indicates organic impurity. But there are many non-pathogenic organisms in the air and soil that can grow in the purest waters and generate minute traces of nitrite. Thus Frankland names the following: *B. ramosus*, *violaceous*, *vermiculars*, *liquidus*, *cereus*, *pestifer*, *plicatus*, *prodigiosus*, *chlorinus*, and *citreus*. Stocklasa adds *subtilis* and *megatherium*, and Burri and Stutzer, *B. denitrificans*. On the other hand, a large number of organisms, some of them pathogenic, reduce nitrite to gaseous nitrogen or to nitrous oxide, acting generally by symbiosis, the intermediate production of nitric acid not being detectable, probably because it is destroyed as fast as it is formed. The pathogenic *B. pyocyaneus* is one of them.

The following are possible conditions: There may be no nitrite, yet pathogenic and other organisms may be present. There may be nitrite with no pathogenic organisms present. In the presence of certain bacteria, the majority of which are harmless, the circumstances may be: (*a*) high free oxygen with nitrite, or (*b*) low free oxygen without nitrite, but with nitrogen and carbon dioxide. If a water is highly aërated and contains nitrites, it is evident that some organism which can form nitrite from ammonia is present, and that such forms as *B. coli* and *B. typhosus* are absent, and in this

case the nitrate would be actually a good sign. In drinking-waters the presence of very small quantities of nitrites may have no significance, and, therefore, reliance on this test alone is objectionable.

Scarlatinal Antitoxin.—Unfortunately it cannot be maintained as yet that serotherapy has been a complete success in more than two or three diseases. The curative treatment of diphtheria—provided it be begun within the first two or three days, and the form be one in which Loeffler's bacilli only are present, or they predominate over Hofmann's and streptococci—and the protection against infection afforded to the susceptible for about a month are almost as perfect as could be wished, and the same may be claimed for one example of the protection afforded by an attenuated virus in variola vaccination; but each has its limits, the latter requiring that the disease shall naturally be one a primary attack of which protects, as a rule, against subsequent exposure for a definite period, whether a month or a lifetime, and the other that the disease shall, unlike tuberculosis, leprosy, or syphilis, be of terminable duration, and for both an animal susceptible to the disease, but possessing far greater powers of resistance than man. So far the only animal that has lent itself successfully to the work is the horse, which has been employed in manufacture of antitoxin for diphtheria and of the various antiplague sera. But Moser, in a paper read before the Annual Congress of German naturalists and physicians held at Carlsbad in September, 1902, described certain experiments conducted by himself with scarlatina. He made cultures of the streptococci from the blood taken from the hearts of sixty-three children, the most virulent cases out of ninety-nine that had died of scarlatina, and inoculated horses with it exactly as in the preparation of diphtheria antitoxin and obtained from them an immunizing serum, with which he inoculated eighty-four children, all whose cases presented a more or less unfavorable prognosis. In all treated on the second day recovery followed, the mortality increasing, as in diphtheria, with each day's delay until, in a few which did not come under his care until the ninth day, it was 50 per cent. The rash disappeared, the temperature and pulse subsided, and the general condition improved with surprising rapidity in all destined to recover, but in the others the improvement was less marked and was not permanent. Marmorek's antistreptococcal serum in his hands proved quite useless.

Pseudovariola.—The epidemic of a pustular or vesicular eruptive fever in Trinidad which the government inspector maintains to be smallpox, though this is stoutly denied by the medical men of the island, and similar outbreaks in other parts of the West Indies and American Continent have led to much discussion. We now find that a like phenomenon has appeared in West Africa. In the Kameruns, as in all parts of the African Continent, smallpox is very prevalent in several forms, and in all highly fatal; but there has recently been reported from Sanaga an outbreak of a pseudovariola in which the eruption, which resembles that of mild smallpox, is preceded by rigors commencing suddenly and fever lasting for from three to eight days, and not followed by pitting. That it was not merely mild smallpox would appear from the fact that of forty children in the Mission School who were attacked thirty-six had been recently vaccinated with calf-lymph.

Dissemination of Typhoid Fever by Shellfish.—Dr. J. T. C. Nash, Medical Officer of Health for Southend-on-Sea, says (*Journal of the Sanitary Institute*, January, 1903, p. 369) that prior to 1900 attacks of typhoid fever were ascribed to the commonly accepted causes and occasionally to shellfish. In 1900 investigation developed the fact that in 25 of the 55 reported cases there was a history of having eaten shellfish within two to three weeks of the onset. Between August 15th and December 31st of the following year 37 cases were reported, and in 21 thereof there was a similar history. During June and July, 1902, 39 cases were reported, in a majority of which there was a history of having handled or eaten, within a month of the onset, cockles which had been laid in a sewage-polluted creek in another district in which, during June, 9 cases of typhoid fever had occurred, which the Medical Officer of Health of the district had reason to believe were due to infected cockles. The creek was inspected, and what was seen was strongly suggestive of organic pollution. The cockle layings were but a quarter of a mile below an outfall of imperfectly purified sewage. Specimens of the cockles were washed twice in pure water, then plunged into boiling water and withdrawn and subjected to examination, which revealed the presence of living sewage. (The survival of the bacteria is readily explained by the fact that several minutes' boiling is required to raise the temperature of the interior of cockles to the thermal death-point of ordinary sewage bacteria.—C. H.) In the discussion of Nash's paper Dr. F. J. Allan, of Westminster, stated that, finding that a patient with typhoid fever had eaten cockles, he had secured some specimens and had submitted them for examination at the Jenner Institute of Preventive Medicine, with the result that typhoid bacilli were isolated.

Dr. R. T. Hewlett (*Journal of State Medicine*, March, 1903, p. 163) relates that on December 5, 1902, four cases of typhoid fever were reported to the Medical Officer of Health for Wandsworth, with evidence that each was due to cockles purchased in the city. Samples of cockles from the same place were examined by Dr. Klein, who found evidence not alone of sewage contamination, but also of the presence of typhoid bacilli. Of eighteen samples of oysters from five different localities, examined at the instance of the Worshipful Company of Fishmongers, eleven were found by the same authority to be contaminated by sewage. Klein and Boyce have shown that oysters contaminated by typhoid bacilli can retain their infective properties for two or three weeks, and it is known that those from sewage-contaminated beds may not be eaten with entire safety until they have lain for about two weeks in unpolluted water. It appears, however, that in cockles the typhoid organism thrives, and that this kind of shellfish is not freed of its infective properties by storage in clean water. Although cockles are not eaten raw, the cooking to which they are subjected is by no means thorough, for boiling for any considerable time makes them tough and uneatable.

The influence of the sewage of a large city is shown by C. A. Fuller (*Science*, 1902, No. 375, p. 363), who collected samples of water and shellfish from various places in Narragansett Bay, into which about 14,000,000 gallons of sewage from Providence, R. I., are discharged daily. Water, oysters, clams, and mussels taken at a distance of a quarter-mile from the sewer outlet yielded *Bacillus coli communis*, *Bacillus cloacæ*, and *Bacterium lactis aërogenes*.

The water and oysters from a bed two miles distant yielded the same organisms. *Bacillus coli communis* was found in 30 per cent. of the oysters and in 60 per cent. of the samples of water from a bed, situated in the line of a strong tidal current five miles away; and in 40 per cent. of the oysters and 70 per cent. of the water samples from another in sluggish water more than five miles away. One bed six miles distant was found to be contaminated, but those farther down than six and a half miles were unpolluted.

These findings are in accord with the statement of DR. E. KLEIN (*British Medical Journal*, February 21, 1903) that the nearer to sewer outlets oysters and cockles are planted the greater the percentage of specimens yielding evidence of pollution. In the examination of oysters he holds that the presence of *Bacillus enteritidis sporogenes* alone is not sufficient proof of recent sewage pollution, but that when the spores of this organism are found together with streptococci and *Bacillus coli communis*, they constitute strong evidence of recent contamination.

DR. HIBBERT W. HILL has recorded (*Report of the Board of Health* of of Boston, Mass., for 1901) interesting results of examination of clams from flats in the immediate vicinity of the sewer outlets of a number of private dwellings. Attention was devoted solely to the bodies of the clams and not to the water contained between the shells, which was practically the same as that which surrounded them. The technique followed was such as to insure absolutely against contamination by bacteria on the surface, and the portion of the body selected as most likely to show infection was the intestine. The following were isolated and identified: *Bacillus coli communis*, *Bacillus enteritidis sporogenes*, and *Bacillus aërogenes capsulatus* (Welch), all three of which are found commonly in sewage. The typhoid bacillus was not found, and it was unlikely to have been present, since the disease existed at the time in but one of the houses, and the excreta of the patient were disinfected. Dr. Hill adds that the search for typhoid bacilli in sewage known to contain them is in most cases practically hopeless, since even in severe epidemics the number of typhoid patients contributing to the sewage is almost always small as compared with the total contributing persons, and only a small proportion of the bacteria present in a typhoid stool are typhoid bacilli; and to hope to find, by examining a few cubic centimetres from a large mass of water, a bacillus which is present in the proportion of one individual to every ten or hundred gallons of water is almost, if not quite, useless.

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